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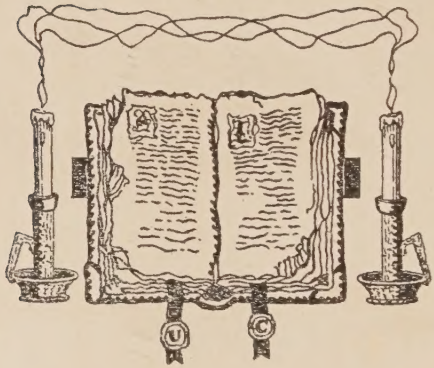

Mrs. F. E. Baldwin
1927

INDICATORS

WORKS OF

DR. I. M. KOLTHOFF

AND

N. HOWELL FURMAN, Ph.D.

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INDICATORS

THEIR USE IN QUANTITATIVE ANALYSIS AND IN THE COLORIMETRIC DETERMINATION OF HYDROGEN-ION CONCENTRATION

BY

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Conservator of the Pharmaceutical Laboratory of the State University, Utrecht.

An Authorized Translation based upon the Second German Edition, revised and enlarged

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NEW YORK

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TRANSLATOR'S PREFACE

THIS edition differs to a considerable extent from the Second German Edition of Dr. Kolthoff's useful treatise. The author has supplied material for a new chapter (the second), which deals with amphoteric compounds from the standpoint of the modern conceptions of Bjerrum.

Numerous other additions, that were also supplied by Dr. Kolthoff, will be found distributed throughout the remainder of the text. Most noteworthy among them are: Data on new sulphone phthalein indicators, p. 61. Extension of the ideas developed in Chapter II to the explanation of the behavior of methyl orange (p. 64), and methyl red (p. 65). Description of a new set of buffer mixtures that can be prepared without the use of standard acid or base (pp. 147 ff). An improvement in the double wedge method (p. 159). Extensive new data on the salt error (pp. 174 ff). New material dealing with measurement of p_H in alcoholic solutions (pp. 184 ff). Revision of the section on distilled water (pp. 188 ff). The Bibliographies of the various chapters and the tables (I–IV) have been brought up to date.

The translator has added author and subject indices, which should greatly enhance the usefulness of the volume.

THE TRANSLATOR.

PRINCETON, N. J.
January, 1926.

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PREFACE TO THE FIRST GERMAN EDITION

The chief uses of indicators are the determination of end-points of neutralizations, and the colorimetric estimation of hydrogen-ion concentration. An indicator which is used in the neutralization of an acid or base must alter its color, or as we usually say "change," at the exact equivalence-point. The concentration of hydrogen ion is not always the same at the equivalence-point; it depends on the dissociation constant of the acid or base with which one titrates. Hence it is not possible to use the same indicator for all neutralizations. The choice of the most suitable indicator is therefore dependent upon the properties of the acids or bases in question. It is advisable to discuss the process of neutralization at length if its full significance is to be grasped. This is done in the first chapter. The relation between the color change of an indicator and the hydrogen-ion concentration is considered in the second chapter. The closely related topic of the use of indicators in neutralizations is treated in Chapter III.

During the past decade indicators have found rapidly increasing use in the determination of hydrogen-ion concentration (*cf.* Chapter V). In Chapter IV we give a full discussion of the manner in which the color of an indicator solution is affected by factors other than the hydrogen-ion concentration. The colorimetric method employs an indirect procedure; the results must therefore be compared with the results obtained by a standard method under strictly comparable conditions. The colorimetric method is well adapted to various uses because of its rapidity.

An indicator paper is an extremely handy device for determining the reaction of a fluid. In the sixth chapter we discuss the properties of these papers, together with the possibility of

their use in the quantitative determination of p_H. Finally, in Chapter VII, we give a brief theoretical résumé of the underlying causes of color change. Hantzsch concluded, as a result of his numerous investigations, that the early theory of Wilhelm Ostwald was decidedly incorrect. Since Ostwald's theory offers very many advantages from a didactic standpoint, his definitions have been altered to such an extent that they no longer contradict the views of Hantzsch. The viewpoint of Julius Stieglitz was extremely useful in this connection.

This treatise makes no pretension of enumerating all of the facts relating to indicators. The organic chemical domain has been omitted from consideration because Thiel's excellent monograph "Der Stand der Indikatorenfrage" (1912) is almost entirely devoted to this subject. Niels Bjerrum has dealt exhaustively with indicators from the physico-chemical side in his excellent paper "Die Theorie der alkalimetrischen und azidimetrischen Titrierungen" (1914). The author is especially indebted to the latter. The excellent treatises of E. B. R. Prideaux, "Theory and Application of Indicators" (1918), and of W. Mansfield Clark, "The Determination of Hydrogen Ions" (1920), did not come to hand until this manuscript was ready for the press. Where it was necessary, the views of these latter authors were considered. Grateful acknowledgment is made of the use of Clark's complete list in compiling the literature summary of Chapter V.

In this treatise an attempt has been made to place the practical use of indicators in the foreground without neglecting theoretical considerations. The author hopes that he has accomplished his purpose, namely: To present a practical manual to all who use the various indicators in titrations, or in the colorimetric determination of hydrogen-ion concentration, without troubling them too much with difficult physico-chemical derivations.

THE AUTHOR.

UTRECHT,
September, 1921.

PREFACE TO THE SECOND GERMAN EDITION

The steadily increasing interest in the investigation of the significance of hydrogen-ion concentration in problems of Chemistry, theoretical and applied, Biochemistry, and Bacteriology, justify the assumption that the first edition of this book filled a real need because, among others, the subject of the simple colorimetric determination of hydrogen-ion concentration was fully discussed. That many found this little volume useful was indicated by the favorable notices in the journals, and the rapid exhaustion of the first edition.

Since the arrangement of the subject matter seemed to be satisfactory from a practical standpoint, it has been left unaltered in preparing the second edition. There are only a few alterations in the text; a large number of additions have been made, the most important of which are enumerated below.

In Chapter I is given a graphic device from which $[H^+]$ may be derived directly from p_H, and conversely. In addition, a graphic method has been adapted from Schoorl. This device enables one to read off the degree of dissociation in solutions of weak acids and bases, given the dissociation constants and concentrations.

The case of acid salts is discussed under the topic of hydrolysis. The calculation of the hydrogen-ion concentration of dibasic acids is considered in the discussion of acids. The important views of Donald D. Van Slyke have been incorporated in the section on Buffer Action, and the strength of the buffering action has been expressed quantitatively as buffer capacity.

Finally, the neutralization curves of mixtures of two acids of different dissociation constants are discussed in the section on neutralization curves at the end of the chapter.

An especially full discussion of the most important properties of indicators is introduced in the second chapter. This is correlated, as far as possible, with the well-known tables of Schultz and Julius. We find repeatedly that a dye which may be used as an indicator is brought on the market in varying degrees of purity. It therefore seemed desirable to give brief descriptions of the indicators to serve as criteria. A full discussion is given of the changes in sensitivity of indicators at higher temperatures. The behavior of indicators in alcoholic solution is detailed in a special section.

In Chapter III special attention is paid to the use of Clark and Lubs' sulphone phthaleins. In a special section there is an account of the titration of mixtures of acids, or of bases with very different dissociation constants.

The fourth chapter, in which the colorimetric determination of hydrogen-ion concentration is explained, has been fully revised in every section.

Various additions have been made, in the fifth chapter, concerning the significance of hydrogen-ion concentration in the different fields of chemistry. The bearing of hydrogen-ion concentration in various fields is explained by examples; reference is given to the literature.

Some new papers are added to the chapter on indicator papers.

Finally, the list of dissociation constants of acids and bases has been extended. Especial attention is called to the fact that many of the values, given in the first edition, of dissociation constants of the alkaloids have been replaced by new ones. An investigation showed that many of the values given in the literature were erroneous even in order of magnitude.

The author will welcome constructive criticisms and requests for further additions.

THE AUTHOR.

UTRECHT,
July, 1923.

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INDICATORS

CHAPTER I

NEUTRALIZATIONS

1. The Principle of Neutralizations.—A quantitative neutralization consists in the determination of the concentration of an acid by titration with a base to form neutral salt. The concentration of a base is determined in a similar manner. If we represent the acid by the expression HA and the base by the formula BOH, the reaction is represented by the equation:

$$HA + BOH \rightarrow BA + H_2O. \quad . \quad . \quad . \quad . \quad (1)$$

According to the electrolytic dissociation theory, electrolytes are partially split into ions in aqueous solution. Hence the acid HA is partially split into H-ions and A-ions, BOH into B-ions and OH-ions, and the salt BA into B-ions and A-ions. Hence equation (1) may be written more appropriately in the form:

$$H^+ + A^- + B^+ + OH^- \rightarrow A^- + B^+ + H_2O. \quad . \quad (2)$$

In other words, A^- and B^+ are not affected by the reaction, since they are present both before and after reaction. The change, therefore, consists solely in the union of H^+ and OH^- to form water:

$$H^+ + OH^- \rightleftarrows H_2O. \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The purest water is dissociated to an extremely small extent into H^+ and OH^-, so that equation (3) must be written as a reversible reaction. When equilibrium has been established we may formulate the mass law expression:

$$\frac{[H^+] \times [OH^-]}{[H_2O]} = K. \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The brackets signify molecular concentrations of the various substances.

If we are dealing with dilute aqueous solutions the concentration of water may be assumed to be constant. Equation (4) then becomes:

$$[H^+] \times [OH^-] = K' = K_{H_2O}. \quad . \quad . \quad . \quad . \quad (5)$$

Equation (5) is of fundamental importance in analytical neutralizations. K_{H_2O} is the *dissociation constant,* or more accurately, the *ionization constant,* or the *ion product* of water. Water dissociates to an exceedingly small extent with simultaneous formation of hydrogen and hydroxyl ions. The ionization constant is very small. It has been determined by various investigators, with excellent agreement. The constant varies strongly with temperature change. The following table gives the values of the dissociation constant of water at various temperatures, according to Kohlrausch and Heydweiller (1).[1]

Dissociation (Ionization) Constant of Water at Different Temperatures

Temperature	K_{H_2O}	p_{H_2O}
0°	0.12×10^{-14}	14.93
18°	0.59×10^{-14}	14.23
25°	1.04×10^{-14}	13.98
50°	5.66×10^{-14}	13.25
100°	58.2×10^{-14}	12.24

2. The Reaction of a Liquid.—In pure water the concentration of hydrogen ion is equal to that of hydroxyl ion. If, for sake of simplicity, we set $K_{H_2O} = 10^{-14}$, then for pure water:

$$[H^+]^2 = [OH^-]^2 = 10^{-14},$$

or

$$[H^+] = [OH^-] = 10^{-7}.$$

Hence 10,000,000 liters of water contain 1 g. hydrogen ion and 17 g. of hydroxyl ion. In acid solutions the concentration of $[H^+]$ is greater than that of $[OH^-]$ and in alkaline solutions the

[1] See also p. 248, Table I.

reverse is true. The product of the two concentrations is constant.

If the value of $[H^+]$ is greater than 10^{-7} we say that the *reaction is acid*. If $[OH^-]$ is greater than 10^{-7}, the solution is *alkaline;* if $[H^+] = [OH^-] = 10^{-7}$, the solution is *neutral.*

We have assumed here that the temperature is 23°, so that $K_{H_2O} = 10^{-14}$.

From equation (5) it follows that:

$$[H^+] = \frac{K_{H_2O}}{[OH^-]}, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and

$$[OH^-] = \frac{K_{H_2O}}{[H^+]}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

When $[H^+]$ is known $[OH^-]$ may be calculated, and conversely. Friedenthal (2) has recommended that the reaction of a solution, even though it be alkaline, be expressed in terms of hydrogen-ion concentration. The $[OH^-]$ may then be calculated with the aid of equation (7).

It has been found more practical for various purposes not to express hydrogen-ion concentration as such, but rather by its negative (Briggsian) logarithm, or by the logarithm of its reciprocal. This proposal is due to Sörensen (3), who calls the number the *hydrogen exponent* and designates it by the symbol p_H. Then we have:

$$p_H = -\log [H^+] = \log \frac{1}{[H^+]}.$$

$$[H^+] = 10^{-p_H}.$$

For example:

$$[H^+] = 10^{-5}, \quad p_H = 5.0.$$

$$[H^+] = 3 \times 10^{-5} = 10^{(\log 3)-5} = 10^{-4.52}, \quad p_H = 4.52.$$

Conversely, corresponding to $p_H = 4.3$ we have

$$[H^+] = 10^{-4.3} = 10^{-5+0.7} = 5 \times 10^{-5}.$$

We may deduce $[H^+]$ graphically from p_H, or the reverse, very simply as shown in Fig. 1. The p_H scale is divided into

ten equal parts from 0.0 to 1.0. The corresponding $[H^+]$ scale is laid off logarithmically. Each decimal of the hydrogen exponent corresponds to the hydrogen-ion concentration value on the lower row. (Fig. 1.)

If we define the hydroxyl exponent in the same manner as the hydrogen exponent, and call the negative logarithm of K_{H_2O} p_{H_2O}, then it follows from equation (5) that:

$$p_H + p_{OH} = p_{H_2O}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

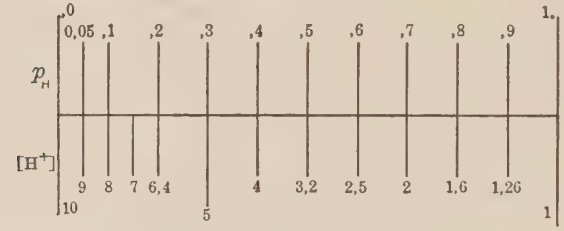

FIG. 1.—Relation between p_H and $[H^+]$.

If K_{H_2O} is 10^{-14}, then p_{H_2O} is 14. Hence from equation (8)

$$p_H + p_{OH} = 14. \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

In pure water $p_H = p_{OH} = 7$. We may therefore define the reaction of a liquid as follows:

$p_H = p_{OH} = 7$	Neutral reaction.
$p_H < 7 < p_{OH}$	Acid reaction.
$p_H > 7 > p_{OH}$	Alkaline reaction.

The smaller the hydrogen exponent the more acid the fluid, and the smaller the hydroxyl exponent the more strongly alkaline is the liquid. A decrease of one unit in hydrogen exponent means a tenfold increase in hydrogen-ion concentration. The use of the hydrogen exponent rather than $[H^+]$ offers especial advantages in graphical representations.

Recently D. Giribaldo, Annales soc. espan. fis. quim. **22**, 555 (1924); Chem. Abst., **19**, 1218 (1925), has proposed that the reaction be expressed by the ratio of $[H^+]$ to $[OH^-]$. This

expression gives large numbers; it is much simplified by using logarithms.

$$\log [H^+] - \log [OH^-] = - p_H + p_{OH}.$$

The expression is zero at neutral reaction; positive when the reaction is acid, and negative with alkaline reaction. A disadvantage is that K_{H_2O} must be known for all cases when this expression is used. Moreover the expression does not give the true acidity, but a relative value. The author does not recommend it for general use.

3. Acids and Bases.—Substances which split off hydrogen ions in aqueous solution are called acids. There are quantitative differences in the strength of the acidic or basic characteristics of the various acids or bases. The greater the degree of dissociation, the stronger is the acid or base in question.

If we denote an acid by HA, it is dissociated as follows:

$$HA \rightleftarrows H^+ + A^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Then, according to the law of mass action:

$$\frac{[H^+] \times [A^-]}{[HA]} = K_{HA} \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

K_{HA} denotes the dissociation constant of the acid and [HA] is the concentration of the undissociated acid. In a pure aqueous solution of an acid $[H^+] = [A^-]$. In such a solution therefore:

$$\frac{[H^+]^2}{[HA]} = \frac{[A^-]^2}{[HA]} = K_{HA},$$

or

$$[H^+] = \sqrt{K_{HA}[HA]} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

This equation is not valid for strong acids. It holds for medium strong and weak acids. If we calculate the degree of dissociation α for a weak acid with the aid of equation (11) we usually find that αc (which is equal to the hydrogen-ion concentration of a pure acid solution) is small in comparison with the total concentration c, so that it may be neglected without great

error. Hence we may substitute for [HA] the total acid concentration c. Equation (12) then becomes:

$$[H^+] = \sqrt{K_{HA} \times c}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

If we wish to calculate p_H, and if we call the negative logarithm of K_{HA} the *acid exponent* p_{HA}, then

$$p_H = \tfrac{1}{2} p_{HA} - \tfrac{1}{2} \log c. \quad . \quad . \quad . \quad . \quad . \quad (14)$$

The following example illustrates the fact that we may set [HA] equal to c in many cases:

The dissociation constant of acetic acid is 1.8×10^{-5} at 18°. Ostwald's dilution law, which may be readily derived, is:

$$\frac{\alpha^2 c}{1 - \alpha} = \frac{\alpha^2}{(1 - \alpha)V} = K_{HA}, \quad . \quad . \quad . \quad . \quad (15)$$

where c represents total acid concentration, α the degree of dissociation:

V is the dilution and is the reciprocal of the concentration, c;

and K_{HA} is the dissociation constant.

In the following table α has been calculated for different concentrations (c) and expressed as per cent of c.

$K_{HA} = 1.8 \times 10^{-5}$

c	100α	$[H^+]$ Calc. by Means of (15)	$[H^+]$ Calc. by Means of (13)	Δ in Per Cent
$\frac{1}{8}$	1.2	1.50×10^{-3}	1.50×10^{-3}	0
$\frac{1}{16}$	1.7	1.06×10^{-3}	1.06×10^{-3}	0
$\frac{1}{32}$	2.4	0.75×10^{-3}	0.75×10^{-3}	0
$\frac{1}{128}$	4.7	0.37×10^{-3}	0.376×10^{-3}	1.5
$\frac{1}{1024}$	12.7	0.12×10^{-3}	0.135×10^{-3}	10

If α is known, the $[H^+]$ is equal to αc and may be calculated rapidly.

One fact which may be derived from the table is that 0.1 N acetic acid is about 1 per cent dissociated into its ions. In cal-

culating the hydrogen-ion concentration of this solution we may assume without appreciable error that the concentration of the undissociated portion is equal to the total concentration. We obtain the same result, i.e., that in 0.1 N solution $[H^+] = 1.35 \times 10^{-3}$, both by the simplified calculation neglecting α (equation 13) and by the more exact calculation including α (equation 15).

Equation (13) retains its validity only in cases where K_{HA} is small and the dilution is not too great. If the degree of dissociation can no longer be neglected we must use equation (12) for the calculation of $[H^+]$; we may write the equation thus:

$$[H^+] = \sqrt{K_{HA}(c - [H^+])}, \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

or

$$[H^+] = -\frac{K_{HA}}{2} + \sqrt{\frac{K^2_{HA}}{4} + K_{HA}c}. \quad . \quad . \quad . \quad (17)$$

It is important to know under what conditions we may use the simple equation (13) for the calculation of the dissociation constant, if we will allow no greater error than about 1 per cent in the derivation.

In the following derivation, use is made of an observation of M. J. E. Verschaffelt (4) in a footnote of a publication by N. Schoorl (4).

According to Ostwald's dilution law we have:

$$\frac{\alpha^2}{(1 - \alpha)V} = K_{HA}, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

hence

$$\alpha^2 = K_{HA}V(1 - \alpha).$$

As a first approximation:

$$\alpha^2 = K_{HA}V,$$

and as a second approximation,

$$\alpha^2 = K_{HA}V(1 - \sqrt{K_{HA}V}),$$

or

$$\alpha = (1 - \tfrac{1}{2}\sqrt{K_{HA}V})\sqrt{K_{HA}V}.$$

If the error is to be smaller than 1, then we must have

$$\tfrac{1}{2}\sqrt{K_{HA}V} < 0.01,$$

or

$$K_{HA}V = \frac{K_{HA}}{c} < 0.0004 < 4 \times 10^{-4}.$$

The limit of usefulness of equation (13) is therefore dependent on the magnitude of the quotient of the dissociation constant divided by concentration. If this is smaller than 4×10^{-4} the value calculated by means of equation (13) will not differ more than 1 per cent from the correct value. If the quotient is greater, the dissociated fraction must be subtracted from the total concentration. The hydrogen-ion concentration is then calculated by means of the quadratic equation (17).

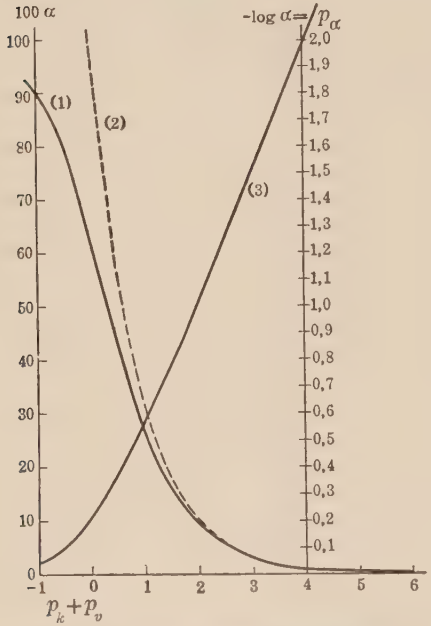

FIG. 2.—Relation between α, K_{HA}, and V.

N. Schoorl (7) has devised a graphic construction with the aid of which one can read off the degree of dissociation of any acid solution (provided Ostwald's dilution law holds) for values given of $K_{HA}V$.

We can deduce from equation (15) that:

$$\alpha = -\tfrac{1}{2}K_{HA}V + \sqrt{\tfrac{1}{4}K^2{}_{HA}V^2 + K_{HA}V}.$$

In this equation α has become a function of KV alone. We may calculate the degree of dissociation α which corresponds to various KV values and assemble the values in a graph. Such a graphic representation is presented in Fig. 2. Instead of

$K_{HA}V$ or K_{HA} we have plotted their negative logarithms, $p_{K_{HA}} + p_V$ or $p_{K_{HA}} - p_c$ on the horizontal axis. The corresponding degree of dissociation may be read off at once from the left-hand ordinate.

The corresponding negative logarithm of α, namely p_α, is given on the right-hand ordinate. The points on curve 1 were calculated from the exact equation; those on the dotted curve 2 by the simple equation (13). We see that both curves coincide when $p_K + p_V$ is greater than 3. From curve 3 one may find $-\log \alpha = p_\alpha$.

EXAMPLE: If $p_{K_{HA}} + p_V$ is equal to 3 (which is the case for 0.02 N acetic acid) then 100α is equal to 3.

If we have read off the value of α from the corresponding value of $p_{K_{HA}} + p_V$, we may derive therefrom the hydrogen exponent. For in every case:

$$\frac{\alpha}{V} = [H^+],$$

$$p_H = -\log \alpha + \log V = p_\alpha - p_V = p_\alpha + p_c.$$

In this equation p_α is the negative logarithm of the degree of dissociation and p_c is the negative logarithm of the concentration.

Hence in 0.02 N acetic acid $p_\alpha = 1.52$ and $p_c = 1.70$, therefore:

$$p_H = 1.52 + 1.70 = 3.22.$$

In the case of a dibasic acid there are two dissociation constants:

$$H_2A \rightleftarrows H^+ + HA^-,$$

$$HA^- \rightleftarrows H^+ + A^=,$$

$$K_1 = \frac{[H^+]\,[HA^-]}{[H_2A]}, \quad \ldots\ldots \quad (19)$$

$$K_2 = \frac{[H^+]\,[A^=]}{[HA^-]}. \quad \ldots\ldots \quad (20)$$

The value of K_1 must be used for the calculation of $[H^+]$ in the solution of a free acid, so that all of the considerations which

have been advanced for monobasic acids hold in this case also. This is especially true for most ordinary cases where the two constants are considerably different, for in this case the second dissociation step is of very minor importance.

When the relations are such that the second stage in the dissociation may not be neglected we may nevertheless calculate the hydrogen-ion concentration in such an acid solution by means of a complicated equation.

The sum of the positive ion concentrations is equal to that of the negative because the solution is electrically neutral. Hence

$$[H^+] = [HA^-] + 2[A^=], \quad . \quad . \quad . \quad . \quad . \quad (21)$$

further

$$[H_2A] = c - [H^+] + [A^=], \quad . \quad . \quad . \quad . \quad (22)$$

where c represents the total concentration of the acid.

It follows from equations (19) and (20) that:

$$[H^+] = \frac{[H_2A]}{[HA^-]}K_1 = \frac{[HA^-]}{[A^=]}K_2,$$

or

$$\frac{[H_2A]\,[A^=]}{[HA^-]^2} = \frac{K_2}{K_1}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (23)$$

As deduced above:

$$[H_2A] = c - [H^+] + [A^=], [A^=] = \frac{[H^+] - [HA^-]}{2},$$

and

$$[HA^-] = \frac{c - [H^+]}{[H^+]}K_1.$$

From these four equations we find that

$$[H^+]^3 + [H^+]^2K_1 - [H^+]\,(K_1c - K_1K_2) = 2K_1K_2c. \quad (24)$$

This equation has various uses. If $[H^+]$ has been determined in two acid solutions of different concentration, we have two equations from which K_1 and K_2 may be found very simply, since they are the only unknowns.

Conversely, we may calculate the hydrogen-ion concentration of a dibasic acid solution if the two constants are known. Although the solution of a third degree equation is not simple,

we may derive the correct value by trial. It is simpler to proceed as follows:

As a first approximation, in the solution of a dibasic acid,

$$[H^+] = [HA^-],$$

because the first dissociation step always takes place to a much greater extent than the second. Hence from equation (19) it is approximately true that:

$$[A^=] = K_2.$$

If we have calculated $[H^+]$ on the assumption that the acid in its pure solution behaves as a monobasic acid, and if K_2 is known, we can at once decide whether it is permissible to disregard the second stage of the dissociation. If we have calculated $[H^+] = 10^{-3}$, for example, and if K_2 is 10^{-6}, the second dissociation step does not need to be considered. On the other hand, if we find that $[H^+]$ is 10^{-4}, and if K_2 is 10^{-5}, then $[A^=]$ is approximately 10^{-5}, and the roughly corrected value of $[H^+]$ is:

$$[H^+] = 10^{-4} + 10^{-5} = 1.1 \times 10^{-4}.$$

The correction is actually smaller because we have assumed that $[H^+]$ is equal to $[HA^-]$, which is not strictly true.

If an approximate value of $[H^+]$ has been found in the above fashion, the exact value may be derived quickly from equation (24).

Illustration: *Phthalic acid:*

$$K_1 = 10^{-3}, \quad K_2 = 3 \times 10^{-6}. \quad c = 0.1:$$

$$[H^+] = 9.5 \times 10^{-3}$$

(it is assumed that phthalic acid acts as a monobasic acid),

$$[A^=] = 3 \times 10^{-6}.$$

The second dissociation step may be neglected.

$$c = 0.001 : [H^+] = 6.2 \times 10^{-4}, \quad [A^=] = 3 \times 10^{-6}.$$

In this case also the second step may be neglected.

Tartaric Acid: $K_1 = 10^{-3}$: $K_2 = 9 \times 10^{-5}$.

$c = 0.1$: $[H^+] = 9.5 \times 10^{-3}$, $[A^=] = 9 \times 10^{-5}$.

The second dissociation step may be neglected.

$c = 0.001$: $[H^+] = 6.2 \times 10^{-4}$ (as a monobasic acid),

$$[A^=] = 9 \times 10^{-5}.$$

The $[H^+]$ corrected approximately for the second dissociation step becomes:

$$[H^+] = 6.2 \times 10^{-4} + 9 \times 10^{-5} = 7.1 \times 10^{-4}.$$

According to equation (24) the exact value is

$$[H^+] = 6.9 \times 10^{-4}.$$

Succinic acid ($K_1 = 6.55 \times 10^{-5}$; $K_2 = 6 \times 10^{-6}$ behaves about like phthalic acid, although the first dissociation constant of the former is only tenfold greater than its second.

The considerations which have been advanced for acids hold equally well for bases, except that in the latter case $[OH^-]$ is calculated. From equation (5) (p. 2) we may derive $[H^+]$ directly.

We will next consider the dissociation constants of the much-used acids and bases, together with their hydrogen-ion concentrations and exponents, p_H, in 0.1 N solution. K_{H_2O} is assumed to be $10^{-14.23}$ at 18°.[2]

The great difference between acidity found by titration, and actual or **true** *acidity, which corresponds to hydrogen-ion concentration,* is very evident in the following table. *The acidity found by titration is equal to the total acid concentration,* and *it is measured by the amount of alkali which is equivalent to the acid.* The acidity, or alkalinity, as found by titration, is the same for all substances in the following table, whereas the actual acidities are very different.

[2] *Cf.* Table III, p. 249 ff.

DISSOCIATION CONSTANTS OF SOME ACIDS AND BASES AT 18°
$[H^+]$ in 0.1 N Solution (4)

	K_1	K_2	K_3	$[H^+]$ in 0.1 N Solution	p_H
Strong acids	Not possible to state	.....	.....	9×10^{-2}	1.05
Carbonic acid	3.04×10^{-7} $10^{-6.52}$	6×10^{-11} $10^{-10.22}$	.....	1.23×10^{-4} (saturated)	3.91
Phosphoric acid	9×10^{-3} $10^{-2.05}$	1.95×10^{-7} $10^{-6.7}$	3.6×10 $10^{-12.44}$	3.04×10^{-2}	1.52
Boric acid	5.5×10^{-10} $10^{-9.26}$	.....	.....	7.41×10^{-6}	5.13
Hydrogen sulphide	6×10^{-8} $10^{-7.22}$	8×10^{-15} $10^{-14.1}$	.....	7.76×10^{-5}	4.11
Acetic acid	1.8×10^{-5} $10^{-4.75}$	.....	.....	1.35×10^{-3}	2.87
Oxalic acid	3.8×10^{-2} $10^{-1.42}$	4.9×10^{-5} $10^{-4.31}$	.....	6.55×10^{-2}	1.18
Phenol	1.0×10^{-10}	.....	.....	3.16×10^{-6}	5.50
Strong bases	Not possible to state	.....	.....	6.6×10^{-14}	13.18
Ammonia	1.7×10^{-5} $10^{-4.77}$	.....	.....	4.42×10^{-12}	11.35
Pyridine	1.6×10^{-9} $10^{-8.80}$	.....	.....	4.68×10^{-10}	9.33
Aniline	3.5×10^{-10} $10^{-9.46}$	.....	.....	1.0×10^{-9}	9.00

4. Hydrolysis of Salts.—When a salt is dissolved in water it is partially decomposed by the water into acid and base. This change is illustrated by the equation:

$$BA + H_2O \rightleftarrows BOH + HA.$$

In the equation BA denotes salt, BOH base, and HA the acid. Since BOH and HA react to form water, the reaction is reversible as indicated above.

It is better to explain hydrolysis by the assumption that the ions of the salt BA react with water. This may be pictured as follows:

$$B^+ + H_2O \rightleftarrows BOH + H^+, \quad . \quad . \quad . \quad . \quad (25)$$

$$A^- + H_2O \rightleftarrows HA + OH^-. \quad . \quad . \quad . \quad . \quad (26)$$

If we consider the salt of a strong acid with an equally strong base, hydrolysis may be completely ignored, because BOH and HA are equally dissociated in dilute solution. The equilibria represented in equations (25) and (26) are displaced completely to the left. The solution has a neutral reaction.

If, on the other hand, we have to deal with the salt of a strong acid with a weak base, or of a weak acid with a strong base, the salt will be hydrolyzed to a notable degree in aqueous solution. In the first case the decomposition represented in equation (26) may be ignored. One may conclude from equation (25) that such a solution will react acid and will contain a certain amount of undissociated base, which is equivalent to the hydrogen-ion concentration. In the second case the solution reacts alkaline and contains an excess of hydroxyl ions together with an equivlent concentration of undissociated acid, HA.

Finally, if we consider the solution of a salt of a weak acid and a weak base, we find that both reactions (25) and (26) take place simultaneously. Although the solution of such a salt, ammonium acetate, for example, may be exactly neutral, it contains, nevertheless, a definite concentration of free undissociated acid and base.

5. Calculation of Hydrogen-Ion Concentration and Degree of Hydrolysis.—(*a*) If we consider the solution of a salt which was formed from a strong base and strong acid, we find that it is not appreciably hydrolyzed. The hydrogen-ion concentration of such a solution is the same as that of pure water, namely 10^{-7}; $p_H = 7$. Actually this would only be the case if the salt were dissolved in exactly neutral water. Practically it is better to say that a "neutral salt" does not change the reaction of water.

(*b*) *Hydrolysis of a Salt of a Weak Acid and Strong Base at Room Temperature.*—As has been stated, the solution of such a salt reacts alkaline, and hence contains an excess of hydroxyl ions. Considering equation (26) it is evident that equivalent concentrations of HA and OH^- are formed by hydrolysis. This is strictly true on the assumption that the base is strong and is completely dissociated. We may apply the law of

mass action to the equilibrium represented in equation (26). We find:

$$\frac{[HA] \times [OH^-]}{[A^-] \times [H_2O]} = K'. \quad . \quad . \quad . \quad . \quad . \quad (27)$$

From this equation, by setting concentration of water equal to a constant we have:

$$\frac{[HA] \times [OH^-]}{[A^-]} = K_{hyd.} \quad . \quad . \quad . \quad . \quad . \quad (28)$$

This constant is called the *hydrolysis constant*, $K_{hyd.}$ We have considered the relations:

$$\frac{[H^+] \times [A^-]}{[HA]} = K_{HA}, \quad . \quad . \quad . \quad . \quad . \quad (11)$$

and

$$[H^+] \times [OH^-] = K_{H_2O}. \quad . \quad . \quad . \quad . \quad . \quad (5)$$

From (11) and (28) it follows that:

$$\frac{[OH^-] \times [H^+]}{K_{HA}} = K_{hyd.},$$

and since

$$[H^+] \times [OH^-] = K_{H_2O},$$

$$K_{hyd.} = \frac{K_{H_2O}}{K_{HA}}. \quad . \quad . \quad . \quad . \quad . \quad (29)$$

It has been stated that in a salt solution [HA] is equal to $[OH^-]$. If the salt is completely ionized $[A^-]$ is equal to c, if c is the total concentration of the salt. From (28) and (29) it follows that:

$$\frac{[OH]^2}{c} = \frac{K_{H_2O}}{K_{HA}},$$

$$[OH^-] = \sqrt{\frac{K_{H_2O} \times c}{K_{HA}}}, \quad . \quad . \quad . \quad . \quad . \quad (30)$$

$$[H^+] = \sqrt{\frac{K_{H_2O} \times K_{HA}}{c}}. \quad . \quad . \quad . \quad . \quad . \quad (31)$$

$$p_{OH} = 7 - \tfrac{1}{2} p_{HA} - \tfrac{1}{2} \log c.^3 \quad . \quad . \quad . \quad (32)$$

[3] If it is only permissible to assume that the salt is partly dissociated, $[A^-]$ equals c, α being the degree of dissociation (or better the activity coefficient),

Since p_H is $14 - p_{OH}$, we find for such a solution:

$$p_H = 7 + \tfrac{1}{2}p_{HA} + \tfrac{1}{2}\log c. \quad . \quad . \quad . \quad . \quad . \quad (33)$$

In calculating the hydrolysis of a solution of a salt of a strong acid and a weak base we find instead of (30) the equation:

$$[H^+] = \sqrt{\frac{K_{H_2O} \times c}{K_{BOH}}}, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (34)$$

$$p_H = 7 - \tfrac{1}{2}p_{BOH} - \tfrac{1}{2}\log c. \quad . \quad . \quad . \quad . \quad (35)$$

Illustration: Desired the hydrogen-ion concentration of a N solution of ammonium chloride. We use in this calculation $c = 1$ and $p_{BOH} = 4.75$.

$$p_H = 7 - 2.375 = 4.625,$$

i.e., $[H^+]$ lies between 10^{-4} and 10^{-5} and equals 2.37×10^{-5}, as has been established by direct measurement.

The degree of hydrolysis of a salt, expressed in per cent of its concentration, is for salts of strong acid—weak base type:

$$\beta = \frac{100\,[H^+]}{c}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (36)$$

When the degree of hydrolysis is very small ($\beta < 1$ per cent), we can not assume that $[BOH] = [H^+]$ (or in the reverse case that $[HA] = [OH^-]$) because the concentration of the hydrogen and hydroxyl ions of water must be considered. The equation from which p_H may be calculated in this case is very complicated, and is better omitted from our consideration (*cf.* Bjerrum, 1914).

(*c*) *Hydrolysis of a Salt of Weak Acid and Weak Base.*—In this instance we must consider the decompositions represented

equation (33) then becomes:

$$p_H = 7 + \tfrac{1}{2}p_{HA} + \tfrac{1}{2}\log \alpha + \tfrac{1}{2}\log c. \quad . \quad . \quad . \quad . \quad . \quad (33a)$$

And equation (35) becomes:

$$p_H = 7 - \tfrac{1}{2}p_{BOH} - \tfrac{1}{2}\log \alpha - \tfrac{1}{2}\log c. \quad . \quad . \quad . \quad . \quad (35a)$$

by both (25) and (26). If the reaction of the solution does not change, equal amounts of undissociated BOH and HA are formed.

$$B^+ + H_2O \rightleftarrows BOH + H^+, \quad . \quad . \quad . \quad . \quad (25)$$

$$A^- + H_2O \rightleftarrows HA + OH^-, \quad . \quad . \quad . \quad . \quad (26)$$

$$H^+ + OH^- \rightleftarrows H_2O. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

It may be immediately deduced from (25) that

$$K_{1\ hyd.} = \frac{K_{H_2O}}{K_{BOH}}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (29)$$

And it follows from (26) that

$$K_{2\ hyd.} = \frac{K_{H_2O}}{K_{HA}}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (29)$$

The hydrolysis constants are therefore inversely proportional to the dissociation constants of the acid and base.

If we consider the salt of an acid and base such that K_{HA} is much greater than K_{BOH}, the aqueous solution must react acid. We can not draw the conclusion from (25) that $[H^+] = [BOH]$, since most of the hydrogen ions are removed by union with A-ions to form HA. Only when the hydrogen ion concentration is not too far removed from 10^{-7}, i.e., when it is not greater than 10^{-6}, are we justified in the assumption that $[BOH] = [HA]$. According to (25) $[H^+]$ and $[BOH]$ should be equal. This is not the case, because the H-ions are removed by formation of HA. If the original hydrogen-ion concentration were unaltered by this process, [BOH] would be exactly as large as [HA], because the hydroxyl ions formed by the hydrolysis would be removed with the formation of BOH. Since the hydrogen-ion concentration is small at the end of the process between (10^{-6} and 10^{-8}) we may assume without great error that the concentrations of the acid and base which form are equal, i.e., $[BOH] = [HA]$. We are now in a position to calculate the hydrogen-ion concentration, the hydrogen exponent, and the

degree of hydrolysis from the usual equations. As was previously shown:

$$\frac{[BOH] \times [H^+]}{[B^+]} = \frac{K_{H_2O}}{K_{BOH}}, \quad . \quad . \quad . \quad . \quad . \quad (34)$$

$$\frac{[HA] \times [OH^-]}{[A^-]} = \frac{K_{H_2O}}{K_{HA}}, \quad . \quad . \quad . \quad . \quad . \quad (29)$$

By multiplication of (29) and (34) we have

$$\frac{[BOH] \times [HA]}{[B^+] \times [A^-]} = \frac{K_{H_2O}}{K_{HA} \times K_{BOH}}.$$

Assuming that the salt is completely dissociated and that its concentration is c, we have $[B^+] = [A^-] = c$. As has been pointed out, $[BOH] = [HA]$. Then we have:

$$\frac{[BOH]^2}{c^2} = \frac{[HA]^2}{c^2} = \frac{K_{H_2O}}{K_{HA} \times K_{BOH}} \quad . \quad . \quad . \quad (37)$$

$$[BOH] = [HA] = c\sqrt{\frac{K_{H_2O}}{K_{HA} \times K_{BOH}}}, \quad . \quad . \quad (38)$$

$$-\log [BOH] = -\log [HA] = -\log c + 7 - \tfrac{1}{2}p_{HA} - \tfrac{1}{2}p_{BOH} \quad (39)$$

If we represent the degree of hydrolysis, expressed in per cent, by β, we have:

$$\beta = \frac{100[BOH]}{c} = 100\sqrt{\frac{K_{H_2O}}{K_{HA} \times K_{BOH}}} \quad . \quad . \quad (40)$$

Since $[BOH]$ is known we may calculate $[H^+]$ simply from (34). Thus:

$$[H^+] = \frac{c}{[BOH]} \times \frac{K_{H_2O}}{K_{BOH}} = \frac{c}{c\sqrt{\frac{K_{H_2O}}{K_{HA} \times K_{BOH}}}} \times \frac{K_{H_2O}}{K_{BOH}}.$$

Rearranging, we have:

$$[H^+] = \sqrt{\frac{K_{H_2O} \times K_{HA}}{K_{BOH}}}, \quad . \quad . \quad . \quad . \quad . \quad (41)$$

$$p_H = 7 + \tfrac{1}{2}p_{HA} - \tfrac{1}{2}p_{BOH}. \quad . \quad . \quad . \quad . \quad (42)$$

We may deduce $[OH^-]$ and p_{OH} in similar fashion. It follows from (40) and (41) that the degree of hydrolysis and the hydrogen exponent are independent of the concentration of salt provided

that it is completely dissociated. If this is not the case, and if α is the degree of dissociation, or activity coefficient, it may be deduced that:

$$[BOH] =]HA] = \alpha c\sqrt{\frac{K_{H_2O}}{K_{HA} \times K_{BOH}}}, \quad . \quad . \quad (38a)$$

$$\beta = 100\alpha\sqrt{\frac{K_{H_2O}}{K_{HA} \times K_{BOH}}}. \quad . \quad . \quad . \quad . \quad (40a)$$

EXAMPLE: We may consider ammonium acetate as a simple illustration. The dissociation constant of acetic acid is $10^{-4.75}$. That of ammonia is the same, i.e., $10^{-4.75}$. It follows from (42) that in a solution of ammonium acetate

$$p_H = 7.0 - 2.37^5 + 2.37^5 = 7.0.$$

A solution of ammonium acetate is *exactly neutral*. The degree of hydrolysis of ammonium acetate in aqueous solution, expressed in hundredths of the concentration is:

$$\beta = 100\sqrt{\frac{10^{-14}}{10^{-9.5}}} = 10^{-0.25} = 0.563 \text{ per cent.}$$

In an 0.1 N ammonium acetate solution the content of undissociated acetic acid and ammonia is about 0.0006 N.

THE HYDROLYSIS OF AMMONIUM FORMATE: Since formic acid is more highly dissociated than ammonia, the solution of their salt has an acid reaction:

$$K_{\text{formic acid}} = 10^{-3.67}; \; K_{NH_3} = 10^{-4.75}.$$

The hydrogen exponent of an aqueous solution of ammonium formate is

$$p_H = 7 + 1.83^5 - 2.37^5 = 6.46.$$

By determining the hydrogen exponent of such a salt solution (which may be done easily with the aid of indicators, as we shall see later) we can readily ascertain whether the solution contains an excess of free acid or base. The hydrolysis of ammonium carbonate is much more complicated (*cf.* Wegscheider (6)).

(*d*) *Hydrolysis of Acid Salts.*—If we consider the salt of

a dibasic acid, BHA, in aqueous solution it is almost completely dissociated in the sense of the equation:

$$BHA \rightleftarrows B^+ + HA^-.$$

The ion HA^- acts as an acid:

$$HA^- \rightleftarrows H^+ + A^=. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (43)$$

In this case we can not set $[H^+] = [A^=]$ as in an ordinary acid solution. Part of the hydrogen ions is used up by the reaction:

$$HA^- + H^+ \rightleftarrows H_2A. \quad . \quad . \quad . \quad . \quad . \quad . \quad (44)$$

From the last two equations it follows at once that:

$$[A^=] = [H^+] + [H_2A]. \quad . \quad . \quad . \quad . \quad . \quad . \quad (45)$$

According to equations (19) and (20) we have:

$$[A^=] = \frac{[HA^-]}{[H^+]}K_2, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (19)$$

and

$$[H_2A] = \frac{[H^+]\,[HA^-]}{K_1}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (20)$$

If we assume that the electrolytic dissociation of the salt BHA is complete, then $[HA^-]$ may be set equal to the total salt concentration c. (If it is not permissible to assume complete dissociation, $[HA^-] = \alpha c$.)

From equations (45), (19) and (20) it may be found that

$$[H^+] = \sqrt{\frac{K_1K_2c}{K_1 + c}}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (46)$$

Noyes (7) was the first to derive an equation of this type.

From the last equation it follows that the concentration of the solution of an acid salt has only a small influence on its hydrogen-ion concentration. This is especially true when K_1 is small in comparison with c. We may write c instead of $K_1 + c$, and equation (46) becomes

$$[H^+] = \sqrt{K_1K_2}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (47)$$

You can always make an approximate calculation of the hydrogen-ion concentration of an acid salt with the aid of the

last equation. The correct value is found if c is 100 fold greater than K_1. In special cases equation (46) must be used.

EXAMPLE: *Sodium Bicarbonate:* $K_1 = 3 \times 10^{-7}$, $K_2 = 6 \times 10^{-11}$.

c = 0.1 molar:

$$[H^+] = \sqrt{K_1 K_2} = 4.35 \times 10^{-9},\ p_H = 8.37.$$

In 0.001 molar solution the same value is found.

Sodium bitartrate: $K_1 = 1 \times 10^{-3}$, $K_2 = 9 \times 10^{-5}$.

c = 0.1 molar:

$$[H^+] = \sqrt{K_1 K_2} = 3 \times 10^{-4},\ p_H = 3.52.$$

c = 0.001 molar:

$$[H^+] = \sqrt{\frac{K_1 K_2 c}{K_1 + c}} = 2.1 \times 10^{-4},\ p_H = 3.68.$$

In the latter case the concentration has a perceptible influence on the reaction of the solution.

6. Hydrolysis at Higher Temperatures.—The equations which have been presented for the equilibria of the products of hydrolysis are also valid at higher temperatures. The degree of hydrolysis and also p_H is dependent upon K_{H_2O} and K_{HA} or K_{BOH}. The influence of heat upon the dissociation constants of many acids and bases is small. Noyes (8) has determined the dissociation constants of acetic acid and ammonia for different temperatures.

t	0°	18°	25°	50°	100°
Acetic acid, K_{HA}	.....	18.2×10^{-6}	.....	.....	11.1×10^{-6}
Ammonium hydroxide, K_{BOH}	13.9×10^{-6}	17.2×10^{-6}	18.0×10^{-6}	18.1×10^{-6}	18.5×10^{-6}

Although we may neglect the change in the dissociation constant of an acid or base under the influence of temperature change, there remains a change in the degree of hydrolysis,

because of the dissociation constant, or more accurately the *ionization constant* of water, increases with temperature rise.

The ionization constant of water is about 100 times as large at 100° as at room temperature.

As was shown previously (p. 16) we may calculate p_H in the solution of a salt of a strong acid and weak base by the equation:

$$p_H = \tfrac{1}{2}p_{H_2O} - \tfrac{1}{2}p_{BOH} - \tfrac{1}{2}\log c. \quad . \quad . \quad . \quad (35)$$

$\frac{1}{2}p_{H_2O}$ is equal to 7 at room temperature, and at 100° it equals 6 approximately. Hence p_H is about one unit smaller at 100° and the reaction is one unit more acid.

Conversely, in the solution of a salt of a weak acid and strong base at 100°, the hydroxyl-ion exponent is smaller by a similar amount. The effect of concentration is of course taken into account.

In solutions of salts of weak acids and weak bases p_H and p_{OH} decrease to about the same extent with increase in temperature.

7. The Reaction in a Mixture of a Weak Acid with its Salt, or a Weak Base with its Salt. Buffer Mixtures or Regulators.— A weak acid is dissociated to a very small extent into ions. If it is under the influence of its salt the dissociation is further repressed by the common ion effect. On the other hand the salt is highly dissociated. We may therefore assume without great error that in the mixture of a weak acid and its salt the [HA] is equal to the total amount of acid, and that the salt is completely dissociated. According to equation (11):

$$\frac{[H^+] \times [A^-]}{[HA]} = K_{HA}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

Hence it follows that:

$$[H^+] = \frac{[HA]}{[A^-]} \times K_{HA}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (48)$$

If [HA] = [A], which is the case if equivalent amounts of acid and salt are present, the hydrogen-ion concentration is equal to the dissociation constant of the acid. It follows from (48) that:

$$p_H = \log C_S - \log C_{Acid} + p_{HA}. \quad . \quad . \quad . \quad (49)$$

C_S denotes salt concentration and C_{Acid} that of acid. p_{HA} is again the negative logarithm of the dissociation constant.

In a similar manner p_{OH} and hence p_H may be calculated for a mixture of a base and its salt.

If we wish to prepare a solution which is strongly acid, we need only dilute the solution of a strong acid to the proper extent. For example, we may prepare a solution of $p_H = 2$ from hydrogen chloride (i.e., 0.01 N HCl). If, however, we wish to prepare a solution of p_H 3 to 7 we cannot do so with sufficient accuracy by this process. If, for example, we wish to prepare an hydrochloric acid solution of $p_H = 6$ we must dilute until the concentration is 10^{-6}, or about millionth normal. Naturally we can not be sure of the value of such a solution. Even a trace of alkali, which the glass vessel might yield, would be sufficient to alter the p_H from 6 to about 8. On the other hand the small amount of carbonic acid which distilled water absorbs from the atmosphere makes the liquid decidedly acid.

Likewise, we can prepare only strongly basic solutions by dilution of the base itself. If we wish to prepare solutions which are feebly alkaline, i.e., with p_H between about 11 and 7, we must proceed in a different manner.

As explained above, we may prepare solutions of desired p_H by mixing a weak acid or base with the salt in appropriate proportions. It follows from equation (48) that small amounts of strong acids or bases have only a slight influence on the p_H of such mixtures; small amounts of alkali from the glass, or of carbon dioxide from the atmosphere, will have no perceptible effect. Sörensen (3) calls these mixtures which resist changes in their reaction "Buffer Mixtures." L. Michaelis (9) coined the name "Regulators"; we might also call them Ampholytes, because they react in an "amphoteric" fashion.

All mixtures of weak acids and their salts or of weak bases and their salts are therefore: Buffer mixtures, or regulators, or ampholytes.

Fels (10) was the first to use such buffer mixtures. They have been very frequently used by Sörensen (3). As we shall see (Chap. V) they are almost indispensable in the colorimetric

determination of hydrogen-ion concentration. We note that the hydrogen- or hydroxyl-ion concentration always lies close to that of the acid or base which is used. If the acid and salt concentrations are equal,

$$p_{\mathrm{H}} = p_{\mathrm{HA}}.$$

If we let the relation of acid to salt equal 100, we have

$$p_{\mathrm{H}} = p_{\mathrm{HA}} - 2.$$

On the other hand if the relation is $\frac{1}{100}$, then

$$p_{\mathrm{H}} = p_{\mathrm{HA}} + 2.$$

It is not permissible to make this relation greater than 100 or less than $\frac{1}{100}$, for the buffer action fails. We may say that in general a buffer mixture, in which p_{H} lies between $p_{\mathrm{HA}} - 1.7$ and $p_{\mathrm{HA}} + 1.7$, may be prepared from an acid and its salt.

The best buffer mixtures are obtained by mixing equivalent quantities of the acid and its salt. We will consider the use of buffer mixtures more thoroughly in connection with the colorimetric determination of hydrogen-ion concentration (Chap. V).

8. Buffer Capacity and Buffer Index.—It is important to express the buffer capacity of a liquid quantitatively for various purposes. Donald D. Van Slyke (11) has presented his views in an important paper entitled "On the Measurements of Buffer-Values and on the Relationship of Buffer-value to the Dissociation Constant of the Buffer and the Concentration and Reaction of the Buffer Solution." We give his views here, in very brief form.

As has been previously stated not all mixtures of a weak acid and its salt have the same capacity to act as buffers—or we should say, rather, they have different buffer intensities. The optimum point of buffer action is at the hydrogen-ion concentration at which the acid is half neutralized.

We may represent the buffer action by a certain unit which we will call the *buffer capacity* or *buffer index*, and to which we will give the symbol π:

$$\pi = \frac{d\mathrm{B}}{d_{p\mathrm{H}}},$$

i.e., π *is the differential quotient of the increasing amount of the base,* B, *expressed in equivalents per liter, over the corresponding change of* p_H. *A solution therefore has a buffer capacity of* 1 *when a liter of its solution alters its reaction one* p_H *unit upon the addition of one equivalent of acid or base.*

In Fig. 3 the amount of B is expressed as ordinate. The values of p_H are given on the abscissa axis. It is evident at once

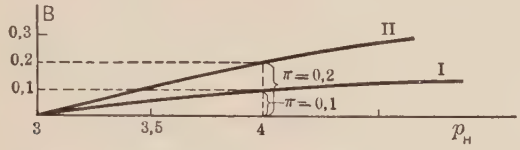

FIG. 3.—Relation between quantity of base, p_H, and buffer capacity.

from the figure that at $p_H = 4$ the buffer capacity is 0.1 curve I and in curve II it is 0.2.

If the line is curved we find the value of the buffer index at any given point by drawing a line tangent at this point and finding the tangent of the angle which the line makes with the abscissa axis.

It is important to determine how large the buffer capacity of different kinds of liquids is.

(*a*) *Buffer Capacity of Water, Strong Acids, and Strong Bases.*— If we add a highly dissociated base to water, dB equals dOH; we may therefore write:

$$\pi = \frac{d\mathrm{B}}{dp_H} = \frac{d\mathrm{OH^-}}{dp_H}.$$

Now we have:

$$p_H = p_{H_2O} - p_{OH}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Hence

$$dp_H = d \log [\mathrm{OH^-}];$$

therefore

$$\pi = \frac{d\mathrm{B}}{dp_H} = \frac{d[\mathrm{OH^-}]}{d \log [\mathrm{OH^-}]} = \frac{[\mathrm{OH^-}]}{0.4343} = 2.3\,[\mathrm{OH^-}]. \quad . \quad (51)$$

Conversely the buffer capacity of water upon adding a strong acid is:

$$\pi = \frac{d\mathrm{B}}{dp_H} = 2.3\,[\mathrm{H^+}]. \quad . \quad . \quad . \quad . \quad . \quad . \quad (52)$$

The total buffer capacity of water to which a strong acid or base has been added is therefore:

$$\pi = 2.3\,([H^+] + [OH^-]). \quad . \quad . \quad . \quad . \quad . \quad (53)$$

If we wish to take account of the incomplete electrolytic dissociation of the strong acid or base, then:

$$\pi = 2.3\left(\frac{[H^+]}{\alpha_{HA}} + \frac{[OH^-]}{\alpha_{BOH}}\right). \quad . \quad . \quad . \quad . \quad (53a)$$

With the aid of equation (53) we may calculate very simply the buffer capacity of solutions of strong acids and bases at various p_H values. Between $p_H = 2.4$ and $p_{OH} = 2.4$ π is smaller than 0.01 and hence in general it is negligible. The

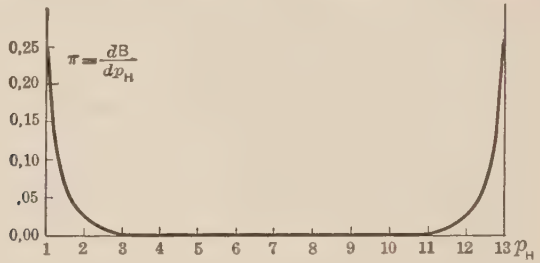

FIG. 4.—Buffer capacity of water with strong acids and bases.

buffer capacity of water solutions of strong acids and bases is presented graphically in Fig. 4. The abscissa represents p_H; the ordinate π.

(*b*) *Buffer Capacity of the Solution of a Weak Acid and its Salt.*—It was shown in equation (48) that in a mixture of a weak acid and its salt

$$p_H = p_{HA} + \log \frac{[A^-]}{[HA]}. \quad . \quad . \quad . \quad . \quad . \quad (54)$$

In general we may set $[A^-]$ equal to the total salt concentration which we designate as C_S[4]; then we have

[4] If we wish to take into account the degree of electrolytic dissociation, we have $[A^-] = \alpha C_S$. Equation (54) may then be written:

$$p_{HA} = p'_{HA} + \log \frac{C_S}{C_{HA}}, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (55a)$$

where

$$p'_{HA} = p_{HA} - \log \alpha.$$

$$p_H = p_{HA} + \log \frac{C_S}{C_{HA}}, \quad . \quad . \quad . \quad . \quad . \quad (55)$$

C_{HA} representing the concentration of acid.

Now C_S is equal to the amount of base, B, which is added in neutralizing acid, hence $[A^-] = C_S = [B]$.

If the original acid concentration was c, then after adding an amount of base [B], it becomes $c - [B]$.

From the equation containing the dissociation constant of the acid we deduce that:

$$[B] = \frac{K_{HA}c}{K_{HA} + [H^+]}.$$

Hence it follows that:

$$\pi = \frac{dB}{dp_H} = -\frac{dB}{d \log [H^+]} = -\frac{[H^+]}{0.4343} \times \frac{dB}{d[H^+]}$$

$$= -2.3[H^+]\frac{dB}{d[H^+]}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (56)$$

By differentiation and further calculation we find finally

$$\pi = \frac{dB}{dp_H} = \frac{2.3[B](c - [B])}{c}. \quad . \quad . \quad . \quad . \quad (57)$$

We may also express buffer capacity as a function of concentration, thus:

$$\pi = \frac{2.3K_{HA}[H^+]c}{(K_{HA} + [H^+])^2} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (58)$$

It follows, therefore, that the buffer capacity increases with increasing concentration of acid. An 0.1 molar acetate mixture has a tenfold greater buffer capacity than an 0.01 molar mixture of the same components.

Joining these conclusions with equation (53), the total buffer capacity of a mixture of weak acid with arbitrary amounts of strong acid or strong base, is given by

$$\pi = 2.3\left\{\frac{K_{HA}[H^+]c}{(K_{HA} + [H^+])^2} + [H^+] + [OH^-]\right\}.$$

The buffer capacities of 0.1 or 0.2 N acetic acid, mixed with strong acid or base, are given in Fig. 5. As may be seen from this figure, we obtain the total buffer capacity between p_H 2 and 3.5 by adding the ordinates of the two dotted curves which represent the buffer capacities of the strong and weak acid, respectively. Outside of these limits we need only deal with the buffer capacity of the weak or strong acid or base, without considering their mutual buffering action.

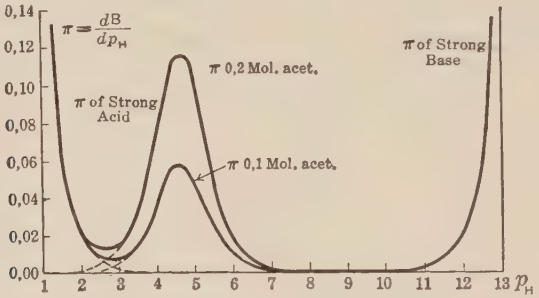

FIG. 5.—Buffer capacity of 0.1 N or 0.2 N mixtures of acetic acid and acetate.

In some instances it is advantageous not to express buffer capacity as such but rather as molecular buffer capacity, π_M, where

$$\pi_M = \frac{\pi}{c}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (60)$$

The curves indicate that the two acetic acid-acetate solutions have their maximum buffer capacity at the same p_H, namely, where $p_H = p_{HA}$. This may be deduced directly from equation (58). If $[H^+] = K_{HA}$, we have

$$\pi = \frac{2.3}{4}c = 0.575c,$$

and

$$\pi_M = 0.575.$$

The buffer action of mixtures of acids or of polybasic acids is given by the following equation:

$$\Sigma\pi = 2.3[H^+]\left\{\frac{K_{H_1A_1}c_1}{(K_{H_1A_1} + [H^+])^2} + \frac{K_{H_2A_2}c_2}{(K_{H_2A_2} + [H^+])^2} + \ldots\right\} + 2.3\,([H^+] + [OH^-]). \quad . \quad (61)$$

If we may assume that the concentrations of the different acids are equal, it follows from the last equation that they have little mutual influence on their buffer capacities provided that their dissociation constants are very different. When the difference between the constants is smaller the mutual effects become greater as is shown in Figs. 6, 7 and 8, and also in the following table.

It is more convenient to write in place of equation (61)

$$\Sigma\pi = \pi_1 + \pi_2 + \pi_3.$$

TABLE. (FIGS. 6, 7, 8)

$p_{H_2A_2} - p_{H_1A_1}$	At $p_H = p_{H_1A_1}$	At $p_H = \frac{p_{H_1A_1} + p_{H_2A_2}}{2}$
3.0	0.577	0.138
2.0	0.598	0.384
1.6	0.684	0.552
1.4	0.749	0.673
1.3	0.784	0.738
1.2	0.848	0.813
1.1	0.919	0.899
1.0	1.003	0.998

The ideas of Van Slyke, which have been detailed, are of importance for various purposes. In the first place, they are of use in the rational preparations of buffer mixtures (see Chap. V), i.e., for liquids of great buffer capacity. The most efficient buffer mixtures are obtained by taking a series of acids whose dissociation constants differ little, so that upon addition of alkali we obtain liquids whose buffer capacity is practically independent of the amount of base added. (*Cf.* Fig. 6.)

Further, in the opinion of the author, buffer capacity curves, which may be deduced readily from neutralization curves, are of great importance in the estimation of the composition of liquids which contain mixtures of various kinds of acids and bases, as for example, soil extracts, beer, milk, fruit juices, foods, etc. Further discussion of these matters is beyond the scope of this treatise.

9. Neutralization Curves.—If we represent graphically the change in hydrogen-ion concentration during the neutralization of an acid or a base we obtain a neutralization curve. It is not easy to represent these curves on ordinary graph paper because the hydrogen-ion concentration varies over such broad limits

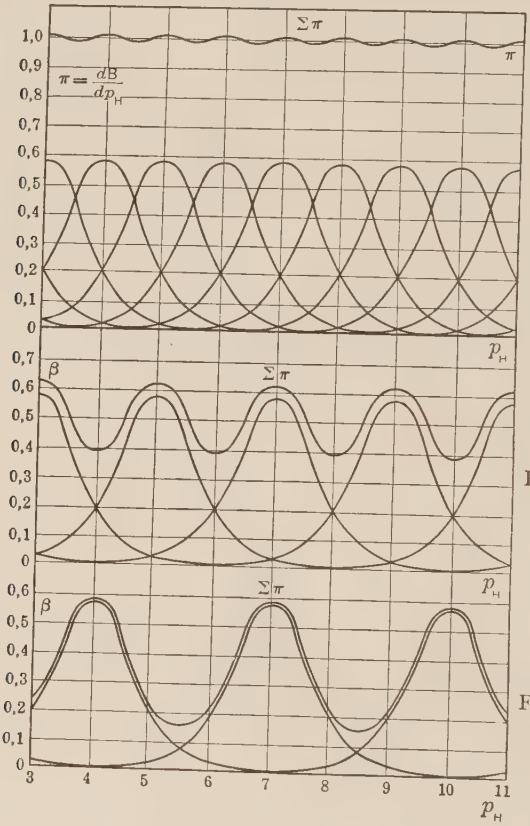

FIG. 6.

FIG. 7.

FIG. 8.

(e.g., for 0.1 N hydrochloric acid from 10^{-1} to 10^{-13} in titration with sodium hydroxide); the hydrogen-ion concentration changes tenfold for each change of 1 in the exponent. Hence only a small portion of the curve can be plotted. Schoorl (loc. cit. 13) has presented the hydrogen-ion concentration changes in the region of the equivalence-point in a very clear schematic fashion. If you wish to gain a clear insight into the course of the neu-

tralization process it is better to plot change in hydrogen exponent rather than change in hydrogen-ion concentration.

The neutralization curves for several kinds of acids and bases will now be presented.

(*a*) *Curve for the Neutralization of a Strong Acid with a Strong Base.*—Let us neutralize 100 cc. 0.1 N hydrochloric acid with alkali at room temperature. In order that the calculation of p_H shall not be too complicated, let us assume that the total volume is unchanged during the neutralization and that the acid is completely dissociated. We find the following values for the course of the neutralization:

100 cc. 0.1 acid 0 cc. 0.1 alkali	$[H^+] = 10^{-1}$,	$p_H = 1.0$
100 cc. 0.1 acid 90 cc. 0.1 alkali	$[H^+] = 10^{-2}$,	$p_H = 2.0$
100 cc. 0.1 acid 99 cc. 0.1 alkali	$[H^+] = 10^{-3}$,	$p_H = 3.0$
100 cc. 0.1 acid 99.9 cc. 0.1 alkali	$[H^+] = 10^{-4}$,	$p_H = 4.0$
100 cc. 0.1 acid 100 cc. 0.1 alkali	$[H^+] = 10^{-7}$,	$p_H = 7.0$
100 cc. 0.1 acid 101 cc. 0.1 alkali	$[H^+] = 10^{-11}$,	$p_H = 11.0$

We see that at the neutralization of 99 per cent of the acid $p_H = 3$, at 99.9 per cent, $p_H = 4$, and at complete neutralization $p_H = 7$. Hence in the neutralization of the last 0.1 per cent of the acid there is an increase of p_H from 4 to 7; there is an equal increase, p_H 7 to 10 when we have added 0.1 per cent more than the equivalent quantity of alkali. It is a simple matter to calculate how large the actual values of p_H are if we take into account the dilution and the degree of dissociation. If the changes in p_H are plotted we obtain curve 1, Fig. 9 (p. 32). Values of p_H are plotted as ordinates. The point 7 is the exact equivalence-point. The amount of acid which has been neutralized is plotted

as abscissa. The abrupt change from 3 to 11, in the curve near the equivalence-point (at 50 acid) is at once evident.

(*b*) *Curve for the Neutralization of a Weak Acid with a Strong Base.*—Let us select acetic acid as an example of a weak acid. As previously mentioned, the dissociation constant is $1.8 \times 10^{-5} = 10^{-4.75}$ at 18°. We may make the assumption that the amount of undissociated acid in an 0.1 N. acetic acid solution is equal to the total concentration (see p. 6). Hence we find a p_H value of 2.87[5] for the solution. On neutralization the acid is changed into highly dissociated acetate. For purposes of calculation we may assume that the salt is completely dissociated. From equation (48) it follows that:

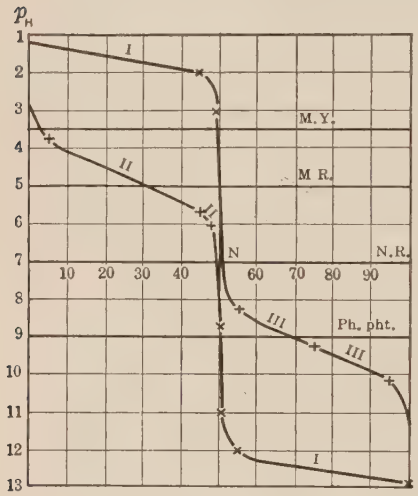

FIG. 9.

$$[H^+] = \frac{[HA]}{[A^-]} \times K_{HA}, \quad \ldots\ldots \quad (48)$$

and from (49):

$$p_H = \log C_{salt} - \log C_{acid} + p_{HA}. \quad \ldots \quad (49)$$

The amount of alkali added corresponds exactly to the amount of salt formed, and is $= C_{salt}$. As was shown in the section on "Hydrolysis," the salt does not react neutral but is alkaline and has a p_H value of 8.87[5] in 0.1 N solution.

If we assume that we start with 100 cc. of 0.1 N acetic acid, and that the total volume does not change during neutralization, and that the salt is completely dissociated, we find the following values for p_H:

100 cc. 0.1 N acetic acid 0 cc. 0.1 N alkali	$p_H = 2.87$
100 cc. 0.1 N acetic acid 10 cc. 0.1 N alkali	$p_H = 3.80$
100 cc. 0.1 N acetic acid 50 cc. 0.1 N alkali	$p_H = 4.75 \ (= p_{HA})$
100 cc. 0.1 N acetic acid 90 cc. 0.1 N alkali	$p_H = 5.70$
100 cc. 0.1 N acetic acid 95 cc. 0.1 N alkali	$p_H = 6.03$
100 cc. 0.1 N acetic acid 100 cc. 0.1 N alkali	$p_H = 8.87$
100 cc. 0.1 N acetic acid 101 cc. 0.1 N alkali	$p_H = 11.0$

Curve II (Fig. 9) gives the change in p_H during the course of the neutralization. We see that this curve coincides with the alkali (sodium hydroxide) curve as soon as the equivalence-point has been passed. Upon addition of alkali to sodium acetate the p_H changes in almost the same way as if the alkali were being added to table salt. We might calculate the values for the neutralization of a strong acid with a weak base in the same way that we have made the calculation for acetic acid and sodium hydroxide. Since this calculation is exactly similar, mutatis mutandis, it is superfluous to include it here. Curve III (Fig. 9) gives the graph of the neutralization of ammonia with hydrochloric acid. After all of the ammonia has been converted into ammonium chloride the curve coincides with the hydrochloric acid curve. Neutralization curves of polybasic acids will be considered in Chapter IV.

(*c*) *Neutralization of a Weak Acid with a Weak Base.*—Since the salts of weak acids and weak bases are in general highly dissociated, we may assume that the amount of base which we add to the acid is equal to the anion concentration. The neutralization curve of a weak acid with a weak base will therefore have initially the same course as that of the neutralization of a weak

acid with a strong base. The course of the curve will be different in the neighborhood of the equivalence-point because of the extensive dissociation of the salt. We give, as an illustration of this case, the calculated changes in p_H during the neutralization of acetic acid with ammonia (13) or the reverse.

The dissociation constants of acetic acid and ammonia are almost equal and have the value of $1.8 \times 10^{-5} = 10^{-4.75}$ at 18°. We have shown that neutral ammonium acetate is about 0.6 per cent hydrolyzed. There is present 0.6 cc. of 0.1 N acetic acid and 0.6 cc. of 0.1 N ammonia in the molecular condition, per 100 cc. of 0.1 N ammonium acetate solution. If 1 cc. of acetic acid is added to 99 cc. of ammonium acetate solution, there is present about 1.6 cc. of acetic acid and 98.4 of the acetate. The repression of hydrolysis is omitted from consideration so that the calculation may not be too complicated. The hydrogen-ion concentration of the mixture is:

$$[H^+] = \frac{1.6}{98.4} \times 10^{-4.75}, \quad p_H = 6.54.$$

The p_H value for mixtures of ammonium acetate and ammonia may be calculated in similar manner.

We may therefore construct a table representing the neutralization of acetic acid with ammonia as follows:

100 cc. acetic acid	
0 cc. ammonia	$p_H = 2.87$
100 cc. acetic acid	
50 cc. ammonia	$p_H = 4.75$
100 cc. acetic acid	
90 cc. ammonia	$p_H = 5.70$
100 cc. acetic acid	
95 cc. ammonia	$p_H = 5.98$
100 cc. acetic acid	
98 cc. ammonia	$p_H = 6.32$
100 cc. acetic acid	
99 cc. ammonia	$p_H = 6.54$

100 cc. acetic acid
100 cc. ammonia $p_H = 7.10$
100 cc. acetic acid
101 cc. ammonia $p_H = 7.66$
100 cc. acetic acid
102 cc. ammonia $p_H = 7.88$
100 cc. acetic acid
105 cc. ammonia $p_H = 8.22$

The course of the p_H values is plotted in curve IV (Fig. 10). We see from the table that the neutral salt reacts exactly neutral, $p_H = 7.1$.

p_{H_2O} was taken as 14.2.

The neutralization curve of acetic acid with ammonia coincides with the curve for acetic acid neutralized with soda up to within about 5 per cent of the equivalence-point. About 5 per cent after the equivalence point is passed it coincides with the hydrochloric acid—ammonia curve. They are strongly divergent only in the neighborhood of the equvialence-point. Hence a large series of buffer mixtures may be prepared by mixing acetic acid and ammonia.

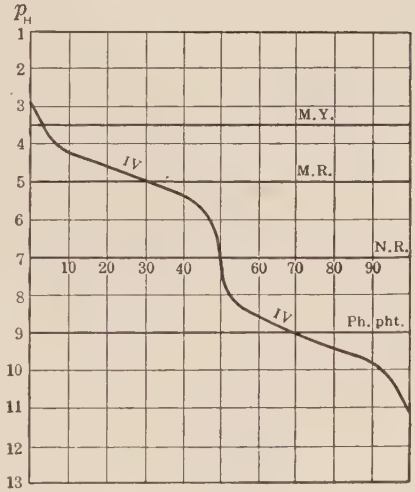

FIG. 10.

(*d*) *The Neutralization of a Mixture of Two Acids.*—In general the calculation of the points on the curve for the neutralization of a mixture of a weak and strong acid does not involve any difficulties. The strong acid is neutralized first upon addition of alkali (*cf.* under *a*) then the weak acid (*cf.* under *b*).

It is more difficult if we have a mixture of a medium strong and a weak acid, as for example, a mixture of acetic and boric

acids. We may include in this classification dibasic acids whose two dissociation constants are very different.

If we call the medium strong acid H_1A_1, and the weak acid H_2A_2, with dissociation constants K_1 and K_2, then it follows from the fundamental equation (11) that in a mixture of the two acids with a certain amount of alkali:

$$[H^+] = \frac{[H_1A_1]}{[A_1^-]}K_1 = \frac{[H_2A_2]}{[A_2^-]}K_2,$$

and that

$$\frac{[H_1A_1]}{[A_1^-]} : \frac{[H_2A_2]}{[A_2^-]} = K_2 : K_1.$$

Now $\frac{[HA]}{[A^-]}$ represents the relation of the concentration of free and neutralized acid. We will call this relation, which is of importance in most analytical calculations which involve neutralization, the *reciprocal neutralization ratio*, in contrast with the quantity $\frac{[A^-]}{[HA]}$, which we will call the *neutralization ratio*. We will make as a first assumption that the concentrations of the acids H_1A_1 and H_2A_2 are equal. If the difference between the the dissociation constants of the two acids is great enough it follows that the stronger acid alone will be neutralized at the beginning of the addition of alkali because the reciprocal neutralization ratio are inversely proportional to the dissociation constants. But in the neighborhood of the first equivalence-point, i.e., the point when an amount of alkali has been added equivalent to H_1A_1, the ability of the second acid, H_2A_2, to consume alkali begins to play a role. At the first equivalence-point the acid H_1A_1 is not completely neutralized while a small portion of H_2A_2 has been converted into salt. The quotients of the reciprocal neutralization ratios may be calculated from the equation last given. If we assume that at the first equivalence-point the acid H_1A_1 is a per cent neutralized, then H_2A_2 must be $(100-a$ per cent) neutralized, since H_1A_1 and H_2A_2 were originally present in equal concentrations.

Hence it follows that $[A_1^-]$ represents a per cent of the total amount of H_1A_1 and $[A_2^-]$ $(100 - a)$ per cent that of H_2A_2.

From the equation last given it follows that:

$$[H^+]^2 = \frac{[H_1A_1]}{[A_1^-]}K_1 \times \frac{[H_2A_2]}{[A_2^-]}K_2. \quad . \quad . \quad . \quad . \quad (62)$$

At the first equivalence-point, therefore:

$$[H^+]^2 = \frac{100 - a}{a} \times \frac{a}{100 - a}K_1K_2,$$

$$[H^+] = \sqrt{K_1K_2}, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (63)$$

$$p_H = \tfrac{1}{2}(p_{K_1} + p_{K_2}). \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (64)$$

If we have a mixture of two bases, then at the first equivalence-point:

$$p_H = p_{H_2O} - \tfrac{1}{2}(p_{K_1} + p_{K_2}). \quad . \quad . \quad . \quad . \quad . \quad (65)$$

It is evident that there is a very simple relation between the hydrogen-ion concentration at the first equivalence-point and the two dissociation constants. Tizard and Boeree (14) have previously derived this relationship; it is made clearer by the computation that has been given.

We have assumed up to this point that the concentrations of the two acids H_1A_1 and H_2A_2 are equal. If this assumption is approximately true there is no practical difference; if, for example, the concentration of H_1A_1 is 10 per cent greater than that of H_2A_2, the change in p_H at the first equivalence-point is scarcely noticeable. A difference is perceptible when the difference between the two concentrations is greater.

Let us assume, for example, that the concentration of H_1A_1 is double that of H_2A_2. Let $[A_1^-] = a$ per cent of the total amount of H_1A_1 at the first equivalence-point, and $[H_1A_1] = (100 - a)$ per cent of the total amount of the first acid and $[H_2A_2] = (2a - 100)$ per cent.

With the aid of equation (62) we find at the first equivalence-point that:

$$[H^+] = \sqrt{\frac{K_1K_2}{2}},$$

$$p_H = \tfrac{1}{2}(p_{K_1} + p_{K_2}) + \tfrac{1}{2}\log 2 = \tfrac{1}{2}(p_{K_1} + p_{K_2}) + 0.15. \quad . \quad (66)$$

In this case the p_H at the first equivalence-point changes only to the extent of 0.15. If the concentration of the first acid is threefold greater, then at the first equivalence-point:

$$p_H = \tfrac{1}{2}(p_{K_1} + p_{K_2}) + \tfrac{1}{2}\log 3 = \tfrac{1}{2}(p_{K_1} + p_{K_2}) + 0.24.$$

If the concentration of H_2A_2 is greater than that of H_1A_1, p_H at the first equivalence-point is smaller by the same amount as is indicated in the above equations.

In Chapter IV we shall see the practical bearing which these considerations have for analytical titrations.

In general the neutralization curve may be derived for any acid with any base provided that the dissociation constants are known. In Chapter IV we shall find that a knowledge of the neutralization curve is necessary for the choice of a suitable indicator.

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CHAPTER II

AMPHOTERIC COMPOUNDS

1. Characteristics of Amphoteric Compounds.—It is characteristic of acids that on solution in water they split off hydrogen ions, while bases on the contrary give hydroxyl ions. But there are numerous compounds that give rise to both hydrogen and hydroxyl ions and hence function both as acids and as bases, although sometimes the acidic and sometimes the basic character may predominate. Therefore these substances are able to take up hydrogen ions as well as hydroxyl ions, and they are said to be **amphoteric**. They might also be called **ampholytes** or **hybrids**. The reaction of the solutions of amphoteric compounds can never be strongly acid or alkaline because of the acidic and basic groups which they contain.

Arsenious acid, aluminium hydroxide, and zinc hydroxide are typical inorganic ampholytes. Organic ampholytes, to which class the amino acids, peptides and proteins belong, are of much greater biological importance.

In general we may represent an amphoteric compound by the symbol HXOH; the amphoteric properties are expressed by the equations:

$$\mathrm{HXOH} \rightleftarrows \mathrm{H^+} + \mathrm{XOH^-} \quad \text{(acid function)},$$
$$\mathrm{HXOH} \rightleftarrows \mathrm{HX^+} + \mathrm{OH^-} \quad \text{(basic function)}.$$

We may apply the law of mass action to both reactions:

$$\frac{[\mathrm{H^+}][\mathrm{XOH^-}]}{[\mathrm{HXOH}]} = k_a,$$
$$\frac{[\mathrm{HX^+}][\mathrm{OH^-}]}{[\mathrm{XHOH}]} = k_b.$$

In addition to the undissociated portion, HXOH, the solution of an ampholyte also contains: $\mathrm{H^+}$, $\mathrm{OH^-}$, anions of the ampholyte $\mathrm{XOH^-}$ and cations of the ampholyte, $\mathrm{HX^+}$.

2. Reaction of the Solution of an Ampholyte.—As has been shown in the section on the hydrolysis of the salt of a weak acid and a weak base (p. 16), the latter can never react strongly acid or alkaline; at least when the ratio between the basic and acidic dissociation constants is not too large or too small. For the same reason an ampholyte solution will never react strongly acid or alkaline, because of the acidic and basic groups which it contains. We are not considering here the case that the ampholyte contains more acid than basic groups, or the reverse, as it then behaves as an acid or a base.

For the sake of simplicity the undissociated part of the ampholyte will be called A; the cation A^+, the anion A^-, whereas the acid dissociation constant is k_a; the basic dissociation constant k_b, and the ion product of water, k_w. The total concentration of the ampholyte is equal to c.

Then:

$$\frac{[H^+][A^-]}{[A]} = k_a, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (67)$$

$$\frac{[OH^-][A^+]}{[A]} = k_b, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (68)$$

$$[H^+][OH^-] = k_w, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (69)$$

$$[A^+] + [H^+] = [A^-] + [OH^-], \quad . \quad . \quad . \quad (70)$$

$$[A] + [A^+] + [A^-] = c, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (71)$$

From (67) and (68) we have:

$$[A^-] = k_a \frac{[A]}{[H^+]}, \quad . \quad . \quad . \quad . \quad . \quad . \quad (72)$$

$$[A^+] = k_b \frac{[A]}{[OH^-]} = \frac{k_b}{k_w}[A][H^+]. \quad . \quad (73)$$

Substituting these values in (70):

$$\frac{k_b}{k_w}[A][H^+] + [H^+] = k_a \frac{[A]}{[H^+]} + \frac{k_w}{[H^+]},$$

and

$$[H^+] = \sqrt{\frac{k_a[A] + k_w}{\frac{k_b}{k_w}[A] + 1}}. \quad . \quad . \quad . \quad . \quad (74)$$

This equation has been derived in a similar way by J. Walker (1). In the equation the values of $[H^+]$ and [A] are unknown and hence it cannot be solved directly.

S. P. L. Sörensen (2) eliminated the unknown [A] and found:

$$[H^+]^4 + [H^+]^3\left(\frac{k_w}{k_b} + c\right) + [H^+]^2\frac{k_w}{k_b}(k_a - k_b) - [H^+]\frac{k_w}{k_b}(k_a c + k_w) - \frac{k_w}{k_b}k_a k_w = 0 \tag{75}$$

This equation is inconvenient for general use. Its general solution can not be given.

The author therefore suggests the general application of equation (74) with the assumption, as a first approximation, that [A] is equal to the total concentration c. Hence we neglect the dissociation of the ampholyte into positive and negative ions, and the value found for $[H^+]$ is a little too high. When this approximate value of $[H^+]$ is known, the corresponding values of $[A^+]$ and $[A^-]$ can be calculated, after which we may apply the correction that:

$$[A] = c - [A^+] - [A^-].$$

The calculation is repeated with this value of [A], and we usually find the correct value for $[H^+]$. If not, the calculation is repeated for the third time; generally the first approximate calculation gives values which are accurate enough.

From equation (74) we see that:

(*a*) The error will become smaller the larger the total concentration c.

(*b*) The error will be smaller, the smaller k_a and k_b are. (*Cf.* the example of phenylalanine.)

(*c*) The ampholyte will behave almost as a monobasic acid when k_a is more than 10^5 times larger than k_b, and c is very small. On the other hand the ampholyte is to be considered as a monacid base when k_b is greater than k_a by the same amount.

EXAMPLES: *Phenylalanine.*—

$$k_a = 2.5 \times 10^{-9}, \quad k_b = 1.3 \times 10^{-12},$$
$$k_w = 10^{-14}, \qquad c = 10^{-2}.$$

According to (74):

$$[H^+] = 3.3 \times 10^{-6},$$

and the corresponding values of

$$[A^-] = 7.3 \times 10^{-6},$$
$$[A^+] = 4. \times 10^{-6}.$$

Therefore the real value of [A] is not equal to 10^{-2}, but to $10^{-2} - 7.3 \times 10^{-6} - 4 \times 10^{-6}$, which is practically the same as 10^{-2}.

In the same way when $c = 10^{-4}$:

$$[H^+] = 5.1 \times 10^{-7},$$
$$[A^-] = 5 \times 10^{-7},$$
$$[A^+] = 0.1 \times 10^{-7}.$$

m-Aminobenzoic Acid:

$k_a = 1.6 \times 10^{-5}$; $k_b = 1.2 \times 10^{-12}$; $k_w = 10^{-14}$; $c = 10^{-2}$.

The first approximation equation (74) gives:

$$[H^+] = 2.7 \times 10^{-4},$$
$$[A^-] = 6. \times 10^{-4},$$
$$[A^+] = 3.3 \times 10^{-4}.$$

The sum of $[A^-]$ and $[A^+] = 9.3 \times 10^{-4}$, whereas it was assumed to be negligible in comparison with $[A] = 10^{-2}$. Upon applying this correction and recalculating we have:

$$[H^+] = 2.5 \times 10^{-4},$$
$$[A^-] = 5.3 \times 10^{-4},$$
$$[A^+] = 2.8 \times 10^{-4}.$$

When $c = 10^{-4}$, the first approximation gives:

$$[H^+] = 4 \times 10^{-5},$$
$$[A^-] = 4 \times 10^{-5},$$
$[A^+]$ = negligible in comparison with $[H^+]$ and $[A^-]$.

The corrected values, twice recalculated, are:

$$[H^+] = 3.2 \times 10^{-5}.$$
$$[A^-] = 3.2 \times 10^{-5}.$$

The same value for $[H^+]$ is obtained if we consider the ampholyte as a monobasic acid.

Some values of the hydrogen-ion concentration of an aspartic

acid solution are given in the following table. The calculations were made: according to the simple equation (74); the corrected values were calculated; and finally the complicated Sörensen formula was used.

Aspartic Acid: $k_a = 1.5 \times 10^{-4}$; $k_b = 1.2 \times 10^{-12}$; $k_w = 10^{-14}$.

Concentration	p_H According to Equation (74)	p_H Corrected	p_H According to Sörensen
∞	2.952	2.952	2.952
1	2.953	2.953	2.954
10^{-1}	2.969	2.973	2.973
10^{-2}	3.083	3.110	3.110
10^{-3}	3.437	3.521	3.521
10^{-4}	3.914	4.165	4.166

We see from the table that the application of the simple equation (74), followed by correcting the value of [A] obtained, always yields exact results.

3. The Isoelectric Point of an Ampholyte.—It is evident from section 2 that every solution of an ampholyte contains certain concentrations of A, A^-, and A^+. In strongly acid solution $[A^-]$ is negligibly small in comparison with $[A^+]$, whereas in strongly alkaline solution $[A^+]$ is negligible in comparison with $[A^-]$. The pure aqueous solution of the ampholyte contains a large excess of [A] as contrasted with $[A^+]$ and $[A^-]$. There must, in fact, be a certain hydrogen-ion concentration at which the concentration of the undissociated part A is a maximum, while the sum of $[A^+]$ and $[A^-]$ is a minimum. This point is called the **isoelectric point** of the ampholyte, because at this point the ampholyte does not migrate in either direction under the influence of the electric current.

According to equations (71), (72) and (73):

$$\frac{c}{[A]} = 1 + \frac{k_a}{[H^+]} + \frac{k_b}{k_w}[H^+]. \quad . \quad . \quad . \quad . \quad (76)$$

According to L. Michaelis (1) we have:

$$d\frac{1}{[A]} = -\frac{k_a}{[H^+]^2} + \frac{k_b}{k_w}.$$

[A] is at a maximum when:

$$-\frac{k_a}{[H^+]^2} + \frac{k_b}{k_w} = 0,$$

or

$$[H^+]_{I.P.} = \sqrt{\frac{k_a}{k_b} k_w} \quad . \quad . \quad . \quad . \quad . \quad . \quad (77)$$

There is thus a very simple relation between the several constants and $[H^+]$ at the isoelectric point. (*Cf.* also H. Eckweiller, H. M. Noyes, and K. G. Falk, and P. A. Levene and H. S. Simms (2); methods for detection of the isoelectric point, cf. L. Michaelis (1); L. Michaelis and I. Nakashima (3); S. P. L. Sörensen (4).)

When the substance contains m acid groups and n basic groups, the hydrogen-ion concentration at the isoelectric point is given by:

$$[H^+]_{I.P.} = \sqrt{\frac{k_{a_1} + k_{a_2} \ldots . + k_{a_m}}{k_{b_1} + k_{b_2} \ldots . + k_{b_n}} k_w} = \sqrt{\frac{\Sigma k_a}{\Sigma k_b} k_w}$$

according to Levene and Simms.

The application of the simple equation (74) to the calculation of the hydrogen-ion concentration of a pure ampholyte solution in which [A] has a high value, and k_a and k_b are at least 1000 times greater than k_w, leads to the expression:

$$[H^+] = \sqrt{\frac{k_a[A] + k_w}{\frac{k_b}{k_a}[A] + 1}} = \sqrt{\frac{k_a}{k_b} k_w} \quad . \quad . \quad . \quad (77)$$

These simplifications lead to the same equations that Michaelis derived for the isoelectric point.

At the isoelectric point therefore:

(*a*) [A] is at a maximum; or the sum of $[A^+]$ and $[A^-]$ is at a minimum.

(*b*) $[A^-]$ is equal to $[A^+]$. This is the real reason why the ampholyte is isoelectric from an electrochemical standpoint.

The equation of Michaelis affords a simple means for the calculation of $[H^+]$ at the isoelectric point if k_a and k_b are known. Some of the values of k_a and k_b, that have been published in the literature, are collected in the following table:

Ampholyte	k_a	Temp.	Author	k_b	Temp.	Author
Alanine	1.9×10^{-10}	25°	Winkelblech (5)	5.1×10^{-12}	25°	Winkelblech (5)
	1.8×10^{-10}	.....	L. J. Harris (6)	2.5×10^{-12}	.....	L. J. Harris (6)
Alanylglycine	1.8×10^{-8}	25°	H. von Euler (7)	2.0×10^{-11}	25°	H. von Euler (7)
	0.66×10^{-8}	.....	L. J. Harris (6)	1.3×10^{-11}	.....	L. J. Harris (6)
Allanylalanine	0.66×10^{-8}	.....	L. J. Harris (6)	1×10^{-11}	.....	L. J. Harris (6)
Arginine, 2nd step	.....	25°	L. J. Harris (6)	2.2×10^{-12}	25°	L. J. Harris (6)
1st step	$<1.1 \times 10^{-14}$	.....	Kanitz (8)	1.0×10^{-7}	.....	Kanitz (8)
2nd step	.....	.....	.....	1.3×10^{-12}	.....	Hunter and Borsook (9)
1st step	1.4×10^{-13}	.....	Hunter and Borsook (9)	1.07×10^{-5}	.....	Hunter and Borsook (9)
Asparagine	8.8×10^{-10}	18°	Lunden (10)	8.8×10^{-13}	.....	Lunden (10)
	1.35×10^{-9}	25°	Lunden (10)	1.5×10^{-12}	.....	Lunden (10)
	3.2×10^{-9}	40°	Lunden (10)	4.2×10^{-12}	.....	Lunden (10)
				1.9×10^{-11}	60°	Walker and Aston (11)
Aspartic Acid	1.5×10^{-4}	25°	Winkelblech (5)	1.2×10^{-12}	25°	Winkelblech (5)
1st step	2.35×10^{-4}	30°	Levene and Simms (12)	1.5×10^{-12}	.....	Levene and Simms (12)
2nd step	3.4×10^{-10}	30°	Levene and Simms (12)			
Betaine	.....	.....	.....	7.6×10^{-13}	25°	Winkelblech (5)
Glycine	3.4×10^{-10}	25°	Winkelblech (5)	2.7×10^{-12}	25°	Winkelblech (5)
	1.2×10^{-10}	17.5°	Michaelis and Rona (13)	1.93×10^{-12}	17.5°	Michaelis and Rona (13)
	1.05×10^{-10}	18°	Dernby (14)	1.7×10^{-12}	18°	Dernby (14)
	1.8×10^{-10}	25°	Harris (6)	2.6×10^{-12}	25°	Harris (6)
				2.8×10^{-11}	60°	Walker and Aston (11)
	1.8×10^{-10}	18°	Tague (15)			
Glycylglycine	1.8×10^{-8}	25°	Euler (7)	2×10^{-11}	25°	Euler (7)
	3.3×10^{-9}	18°	Dernby (14)	0.95×10^{-11}	18°	Dernby (14)
	5.3×10^{-9}	25°	Harris (6)	1.4×10^{-11}	25°	Harris (6)
Glutamic acid, 2nd step	1.6×10^{-10}	25°	Harris (6)			
1st step	6.3×10^{-5}	25°	Harris (6)			
1st step	6.3×10^{-5}	25°	Holmberg (16)			

1st step	6×10^{-5}	18°	Tague (15)			
Histidine, 2nd step	.....	.....	.....	5.0×10^{-13}	25°	Kanitz (8)
1st step	2.2×10^{-9}	25°	Kanitz (8)	5.7×10^{-9}	25°	Kanitz (8)
Leucine	1.8×10^{-10}	25°	Winkelblech (5)	2.3×10^{-12}	25°	Winkelblech (5)
	2.5×10^{-10}	25°	Harris (6)	2.3×10^{-12}	25°	Harris (6)
Leucylglycine	1.5×10^{-8}	25°	Euler (7)	3.0×10^{-11}	25°	Euler (7)
Lysine, 2nd step	.....	.....	.....	1.1×10^{-12}	25°	Kanitz (8)
1st step	1.2×10^{-11}	25°	Kanitz (8)	$>1.1 \times 10^{-7}$	25°	Kanitz (8)
2nd step	.....	.....	.....	1.0×10^{-12}	25°	Harris (6)
1st step	2×10^{-11}	25°	Harris (6)	3.2×10^{-5}	25°	Harris (6)
Phenylalanine	2.5×10^{-9}	25°	Kanitz (8)	1.3×10^{-12}	25°	Kanitz (8)
	7.5×10^{-10}	25°	Harris (6)			
	7.5×10^{-10}	25°	Tague (5)			
Tyrosine	4.0×10^{-9}	25°	Kanitz (8)	2.6×10^{-12}	25°	Kanitz (8)
2nd step	4.0×10^{-11}	25°	Harris (6)			
1st step	4.0×10^{-10}	25°	Harris (6)			
1st step	7.0×10^{-10}	18°	Tague (15)			
Valine	.....	.....	.....	2.0×10^{-12}	25°	Harris (6)
Arsenious acid	6×10^{-10}	25°	Wood (17)	1×10^{-14}	25°	Wood (17)
Cacodylic acid	6.4×10^{-7}	25°	Johnston (18)	3×10^{-13}	25°	Zawidski (19)
	7.5×10^{-7}	25°	Holmberg (16)	5.6×10^{-13}	25°	Holmberg (16)
Caffeine	$<1 \times 10^{-14}$	25°	Wood (17)	4.0×10^{-14}	25°	Wood (17)
Theobromine	1.3×10^{-8}	18°	Paul (20)	1.3×10^{-14}	18°	Paul (20)
	1.1×10^{-10}	25°	Wood (17)	4.8×10^{-14}	40°	Wood (17)
Theophylline	1.7×10^{-9}	25°	Wood (17)	1.9×10^{-14}	25°	Wood (17)
m. Aminobenzoic acid	1.6×10^{-5}	25°	Michaelis and Davidsohn (21)	1.2×10^{-11}	25°	Michaelis and Davidsohn (21)
	1.6×10^{-5}	18°	Winkelblech (5)	1.2×10^{-11}	.....	Winkelblech (15)
o. Aminobenzoic acid	1.06×10^{-5}	18°	Lunden (10)	1.37×10^{-12}	18°	Lunden (10)
o. Aminobenzoic acid	1.35×10^{-5}	40°	Lunden (10)	3.15×10^{-12}	40°	Lunden (10)
p. Aminobenzoic acid	1.2×10^{-5}	25°	Winkelblech (5)	2.3×10^{-12}	25°	Winkelblech (15)
p. Aminobenzoic acid	1.2×10^{-5}	25°	Michaelis and Davidsohn (21)	2.3×10^{-12}	25°	Michaelis and Davidsohn (21)

4. Neutralization Curve of Ampholytes.—When a strong acid is added to the solution of an ampholyte, the concentration of the cations $[A^+]$ will increase, while that of the anions will decrease. When the excess of acid is sufficient, the concentration of the anions $[A^-]$ is so small that it is negligible. We may then consider the ampholyte only as a weak base and calculate the rest of the neutralization curve on this basis. In the same manner the ampholyte may be considered as a weak acid, without taking into account its basic properties, when an excess of strong base has been added such that the concentration of the cation $[A^+]$ is negligible in comparison with the concentration of the anion, $[A^-]$.

The calculations are more complicated in the neighborhood of the isoelectric point, and we must consider both the basic and acidic properties of the ampholyte.

Let us consider an ampholyte whose acid dissociation constant k_a is larger than the basic constant, k_b, as is usually the case. Let the total concentration of the ampholyte be c; an amount of HCl corresponding to a concentration, a, is added. Further, it is assumed that the salt formed is completely dissociated. Then since the sum of the cation concentrations is equal to that of the anions:

$$[H^+] + [A^+] = [A^-] + [Cl^-] + [OH^-] = [A^-] + [Cl^-] = [A^-] + a$$

or

$$[A^+] = [A^-] + a - [H^+]. \quad . \quad . \quad . \quad . \quad (78)$$

Moreover we have:

$$[A^+] = \frac{[A]}{[OH^-]} k_b = \frac{k_b}{k_w} [A] [H^+], \quad . \quad . \quad . \quad (73)$$

and

$$[A^-] = \frac{[A]}{[H^+]} k_a. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (72)$$

By combining these equations:

$$\frac{k_b}{k_w} [A] [H^+] = a - [H^+] + \frac{[A]}{[H^+]} k_a.$$

$$[H^+]^2 - [H^+] \frac{a}{\frac{k_b}{k_w}([A] - a) + 1} - \frac{([A] - a)k_a}{\frac{k_b}{k_w}([A] - a) + 1} = 0,$$

$$[H^+] = \frac{a}{2\left\{\frac{k_b}{k_w}([A] - a) + 1\right\}} + \sqrt{\left\{\frac{a}{2\frac{k_b}{k_w}([A] - a) + 1}\right\}^2 + \frac{([A] - a)k_a}{\frac{k_b}{k_w}([A] - a) + 1}} \quad . \quad (79)$$

In solving this equation it is again assumed that [A] is equal to c, just as was done in the calculation of $[H^+]$ in the solution of a pure ampholyte. If the deviation is too great the calculation is repeated using for [A] a value of $c - [A]$. The equation above is rather complicated. In many practical instances simplifications may be made. It lies beyond the scope of this book to enter into further details.

A similar equation may be derived in case a base is added to the solution of an ampholyte. The author wishes to emphasize the fact that the complicated formula need only be applied in the neighborhood of the isoelectric point. At other hydrogen-ion concentrations we may apply the simple equations for univalent bases or acids. Equation (78) yields the important information that the amount of acid necessary to bring an ampholyte solution in water to the isoelectric point is equal to the difference between $[H^+]$ at the isoelectric point and that of the solution.

5. Hybrid Ions. (Zwitterionen.) Theory of N. Bjerrum.—Bredig (22) was the first to suggest that an ampholytic substance is an internal salt and therefore contains both a positive and a negative electric charge within the same molecule. F. W. Küster (23) suggested, in explanation of the behavior of methylorange as an indicator, that the free acid should be considered as being mainly a "Zwitterion" (*cf.* page 64). In the literature it has generally been assumed that the formation of these hybrid ions could only take place to a small extent. Even L. Michaelis (24) in dealing with the hybrid ions of amino acids says: "Their amounts are probably always vanishingly small."

A very great service has been rendered by N. Bjerrum (25) in showing that most amino acids in water solution are to be considered as hybrid ions. As will be shown later, the behavior of amino acids is readily explainable on this assumption.

In order to elucidate the hybrid-ion theory we will compare ammonium acetate with an amino acid whose acidic and basic dissociation constants are the same as those of acetic acid and ammonia, respectively. We know that an 0.1 molar solution of ammonium acetate is hydrolyzed to the extent of about 0.5 per cent, and that 99.5 per cent of the salt is dissociated into its ions. Using the same equations, calculations show that our special amino acid will be about 0.5 per cent hydrolyzed, and it is logical to assume that the remainder will be present in the iogenic form. But this internal salt can not split up into ions because the charges are bound to special groups within the whole molecule. According to this conception a small part of an amino acid, NH_2RCOOH, is hydrolyzed into the cations, $^+NH_3RCOOH$, and the anions, NH_2RCOO^-, but the largest portion remains in the form of the internal salt,

$$^+NH_3RCOO^- \text{ (hybrid ion)},$$

whereas according to the old conception the non-hydrolyzed portion consists of the neutral molecules, NH_2RCOOH.

The author's calculations in the former sections are based on the latter assumption, although it appears to be false. As we shall see below, the results of the calculations are correct, although the interpretation of the values of the acid and basic dissociation constants is incorrect. If we call the undissociated amino acid, NH_2RCOOH, A, and the hybrid ions $^+A^-$; the cation A^+, and the anion A^-, we have according to the old conception:

$$\frac{[H^+][A^-]}{[A]} = k_a, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (67)$$

$$\frac{[A^+][OH^-]}{[A]} = k_b. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (68)$$

According to the modern conception:

$$\begin{aligned} ^+NH_3RCOOH &\rightleftarrows {}^+NH_3RCOO^- + H^+, \\ \mathbf{A}^+ &\rightleftarrows {}^+A^- + H^+, \end{aligned}$$

or

$$\frac{[^+A^-][H^+]}{[A^+]} = K_a, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (80)$$

and

$$\begin{aligned} H_2O + NH_2RCOO^- &\rightleftarrows {}^+NH_3RCOO^- + OH^-, \\ A^- &\rightleftarrows {}^+A^- + OH^-, \end{aligned}$$

and

$$\frac{[^{+}A^{-}][OH^{-}]}{[A^{-}]} = K_b. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (81)$$

K_a and K_b are the true dissociation constants of the acidic and basic groups, whereas k_a and k_b are apparent dissociation constants.

There is a very simple relation between k_a, k_b, K_a, and K_b. Since [A] according to the old conception is equal to $[^{+}A^{-}]$ on the new basis, by multiplication of equations (68) and (80) and introducing the value of the ionization constant of water, we have:

$$K_a = \frac{k_w}{k_b}, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (82)$$

and from equations (67) and (81),

$$K_b = \frac{k_w}{k_a}.$$

From the above we see that the true acid dissociation constant of the amino acid is nothing else but the hydrolysis constant of the apparent basic dissociation constant k_b; and the true basic dissociation constant corresponds to the value of the hydrolysis constant of the acid group according to the old theory. The great difference between the old and new conceptions is that the basic character according to the old view is really expressed by the acid dissociation constant, as shown by Bjerrum's theory which has been described. The acid character is really expressed by the basic dissociation constant of the old theory.

When a strong acid is added to an amino acid, we have, according to the old theory:

$$NH_2RCOOH + H^{+} \rightleftarrows {}^{+}NH_3RCOOH;$$

according to the new theory:

$${}^{+}NH_3RCOO^{-} + H^{+} \rightleftarrows {}^{+}NH_3RCOOH.$$

On the old conception the basic NH_2 group is neutralized by the strong acid, while according to the modern conception the weak acid $^{+}NH_3RCOOH$ is liberated from the salt $^{+}NH_3RCOO^{-}$. In this respect we may compare the behavior with ammonium acetate:

$$NH_4^{+} + CH_3COO^{-} + H^{+} \rightleftarrows NH_4^{+} + CH_3COOH.$$

Upon treatment of an amino acid with hydroxyl ions the weak base NH_2RCOO^- is liberated, just as ammonia is liberated from its salts by an excess of base:

$$^+NH_3RCOO^- + OH^- \rightleftarrows NH_2RCOO^- + H_2O.$$

There is a complete analogy between the behavior of an amino acid toward acids and bases, and that of a salt such as ammonium acetate, with this restriction: that the hybrid ion does not conduct the electric current, whereas the ammonium and acetate ions, with their free charges, of course conduct.

In the following table the values of k_a, k_b, K_a, and K_b of amino acids at 25°, as calculated by Bjerrum, are given.

Dissociation Constants of Amino Acids (N. Bjerrum)

	k_a	k_b	K_a	K_b
Glycine	$10^{-9.75}$	$10^{-11.57}$	$10^{-2.33}$	$10^{-4.15}$
Methylglycine	$10^{-9.89}$	$10^{-11.75}$	$10^{-2.15}$	$10^{-4.01}$
Dimethylglycine	$10^{-9.85}$	$10^{-11.97}$	$10^{-1.93}$	$10^{-4.05}$
	About			
Betaine	10^{-14}	$10^{-12.66}$	$10^{-1.34}$	About 1
Alanine	$10^{-9.72}$	$10^{-11.29}$	$10^{-2.61}$	$10^{-4.18}$
Leucine	$10^{-9.75}$	$10^{-11.64}$	$10^{-2.26}$	$10^{-4.15}$
Phenylalanine	$10^{-8.60}$	$10^{-11.89}$	$10^{-2.01}$	$10^{-5.30}$
Tyrosine	$10^{-8.40}$	$10^{-11.39}$	$10^{-2.51}$	$10^{-5.50}$
Glyclglycine	$10^{-7.74}$	10^{-1} .70	$10^{-3.20}$	$10^{-6.16}$
Alanylglycine	$10^{-7.74}$	$10^{-10.70}$	$10^{-3.20}$	$10^{-6.16}$
Leucylglycine	$10^{-7.82}$	$10^{-10.52}$	$10^{-3.38}$	$10^{-6.08}$
		About		
Taurine	$10^{-8.8}$	10^{-14}	About 1	$10^{-5.1}$
Asparagine	$10^{-8.87}$	$10^{-11.82}$	$10^{-2.08}$	$10^{-5.03}$
Lysine, 1st step	10^{-12}	$<10^{-6.96}$	$10^{-1.94}$	$10^{-1.9}$
2nd step	.....	$10^{-11.96}$	.....	$10^{-6.96}$
Arginine, 1st step	$<10^{-13.96}$	$10^{-7.0}$	$10^{-2.24}$	>1
2nd step	.....	$10^{-11.66}$	.....	$10^{-6.9}$
Histidine, 1st step	$10^{-8.66}$	$10^{-8.24}$	$10^{-1.60}$	$10^{-5.24}$
2nd step	.....	$10^{-12.30}$	.....	$10^{-8.24}$
Aspartic acid, 1st step	$10^{-3.82}$	$10^{-11.92}$	$10^{-1.98}$	$10^{-1.8}$
2nd step	$10^{-12.1}$	.....	$10^{-3.82}$	

6. Advantages of the "Hybrid" Conception.—According to the old theory the acid dissociation constant, k_a, usually has values between 10^{-8} and 10^{-10}, which is very improbable as all

of them (excepting taurine) are carboxylic acids, which have dissociation constants between 10^{-5} and 10^{-2}. The true acid dissociation constants of the amino acids lie between $10^{-1.1}$ and $10^{-3.5}$. These true dissociation constants are somewhat higher than those of the common carboxylic acids. This is to be expected, however, because the positively charged amino group of the amino acid will favor the splitting off of hydrogen ions, and will therefore increase the acid character. The nearer the amino group is situated to the carboxylic group the greater is the effect. In glycine for example, K_a is $10^{-2.33}$, whereas in glycylglycine where the amino group is at a greater distance from the carboxylic group, K_a is $10^{-3.20}$. Similar considerations hold true for the basic dissociation constant, which is $10^{-4.15}$ for glycine, and $10^{-6.16}$ in case of glycylglycine.

The behavior of sulphonic acids is also explained by the new theory. These belong to the strong-acid class, and may be compared with sulphuric acid. Now in taurine k_a is as small as $10^{-8.8}$, which in incomprehensible. According to the hybrid theory K_a is about 1, which is in excellent agreement with its behavior as a sulphonic acid.

The behavior of methyl orange as an indicator can only be explained in terms of the new theory. (*Cf.* page 64. (26).) It seems to the author that very good evidence in favor of the hybrid theory lies in the fact that Walbum (4) noted a very large temperature coefficient of k_a for glycine. Now we know that carboxylic acids and ammonia have a very small temperature coefficient. Upon recalculating Walbum's data on the new basis it is found that K_b is increased only two-fold between 10° and 70°.

The behavior of amino acids in other cases, as for example, the mustard oil reaction, the formaldehyde titration, etc., can only be easily understood on the basis of the new conception.

7. Equilibrium between the Amino Acid and Hybrid Ion.—A solution of an amino acid contains both the free amino acid and the hybrid ion.

$$NH_2RCOOH \rightleftarrows {}^{+}NH_3RCOO^{-}.$$

$$\frac{[{}^{+}A^{-}]}{[A]} = n.$$

The value of n can only be roughly approximated. In the cases: dimethylglycine, glycine, and phenylalanine, Bjerrum calculates that n is equal to 10^4; for glycylglycine, 10^2. In these cases we may tacitly assume that all of the amino acid is present in the hybrid-ion form. This is no longer possible in dealing with aromatic amino acids such as derivatives of benzoic acid. In this connection the reader is referred to Bjerrum's paper (25). We will not attempt further discussion as very little is known regarding this question.

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CHAPTER III

THE COLOR CHANGE OF INDICATORS

1. Definition.—According to Wilhelm Ostwald, indicators are weak acids or bases which have one color in the undissociated condition, and another color when ionized. Hantzsch and others have shown that color change is caused by change in constitution rather than by ionization. Ostwald's explanation is still the more convenient for the elucidation of the behavior of indicators at various hydrogen-ion concentrations. We will return later (Chapter VIII, page 233) to the views of Ostwald and Hantzsch. It will be shown that Hantzsch's conception extends Ostwald's views, but does not replace them. We shall see that it is advisable to alter Ostwald's definition somewhat, and to state that: *Indicators are acids or bases whose iogenic form is of constitution and color different from those of the pseudo- or normal form.*

2. Color Change of Indicators and p_H Interval of Change.—If we consider an indicator as an acid, it will be dissociated to a certain degree into ions, in aqueous solution. If we call the indicator acid HIn, the ionization is represented by the equation:

$$HIn = H^+ + In^-. \quad . \quad . \quad . \quad . \quad . \quad . \quad (83)$$

HIn represents the acid form and In^- the alkaline form. The quantitative relations are given by the following equation:

$$\frac{[H^+]\,[In^-]}{[HIn]} = K_{HIn}, \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (84)$$

It follows therefore that:

$$\frac{[In^-]}{[HIn]} = \frac{K_{HIn}}{[H^+]}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (85)$$

If K_{HIn}, $= [H^+]$, then $[In^-] = [HIn]$, and the indicator has been half transformed into its alkaline form. It follows from equation

(85) that the relation between the acid and alkaline forms is a function of the hydrogen-ion concentration. It is incorrect, therefore, to speak of the transition point of an indicator, since it does not change over suddenly from one form to the other at a definite hydrogen-ion concentration. The color change takes place gradually, as may be seen from equation (85), when the hydrogen-ion concentration is of about the same order of magnitude as the dissociation constant. At every value of the hydrogen-ion concentration a certain part of the indicator is present in both acid and alkaline forms. Since only a limited amount of one form can be perceived in the presence of the other, the "change" of the indicator falls within certain values of hydrogen-ion concentration. If we express the two limits of the perceptible change in p_H, then the region between the two limiting values is the interval of change, or *the transition interval* of the indicator. The magnitude of this interval is not the same for all indicators because the color of the acid or alkaline portion is more sensitively distinguished, in the presence of the other portion, in some cases than in others.

If we assume that in a given case 10 per cent of the alkaline form must be present in order to be visible in the presence of the acid form, we have:

$$\frac{[In^-]}{[HIn]} = \frac{K_{HIn}}{[H^+]} = \tfrac{1}{10}.$$

Then

$$[H^+] = 10 \times K_{HIn},$$

and

$$p_H = p_{HIn} - 1. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (86)$$

The expression HIn denotes the negative logarithm of K_{HIn}. If we make the further assumption that the indicator is practically completely converted into the alkaline form when about 91 per cent is present in this form, we have:

$$\frac{[In^-]}{[HIn]} = \frac{K_{HIn}}{[H^+]} = 10.$$

Then

$$[H^+] = \tfrac{1}{10} \times K_{HIn},$$

and

$$p_H = p_{HIn} + 1. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (87)$$

According to (86) the change of the indicator begins at a p_H which is about 1 unit smaller than p_{HIn}; it is practically complete when p_H is about 1 unit larger than p_{HIn}. The transition interval in this instance is about 2 hydrogen-ion concentration units. The range is actually 2 units for most indicators. If the acid form is as distinctly perceptible in the presence of the alkaline form as in the reverse instance, then the color alters equally for equal changes in p_H, both above and below p_{HIn}. If a graph

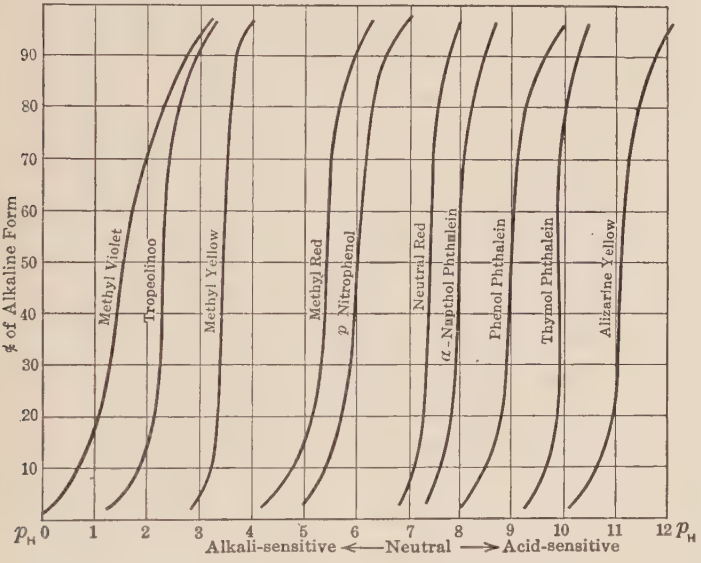


FIG. 11.—Transition ranges of indicators.

is constructed to show the amount of the alkaline form that is obtained at various values of the hydrogen exponent, a bilogarithmic curve is obtained. The branches above and below the 50 per cent ordinate are symmetrically placed with respect to each other. Fig. 11 presents such curves, the p_H values being laid off on the abscissa axis, the amount in the alkaline form on the ordinate axis. Each curve becomes asymptotic to the abscissa axis because at every value of p_H there is a certain amount of the acid form present with the basic form, or vice versa (*Cf.* also the table at the end of the book).

Bjerrum (1) first used such curves to present the change of a certain indicator graphically. Clark and Lubs (2) then showed graphically how the dissociation (α) changes at various p_H values. The latter mode of presentation is not as clear because the curves run from the lower left to upper right, or from lower right to upper left of the diagram, depending upon whether we are dealing with an acidic or basic indicator substance. Curves of the kind shown in Fig. 11 all have analogous forms. The value for p_{HIn} may be very simply read from such a curve, since

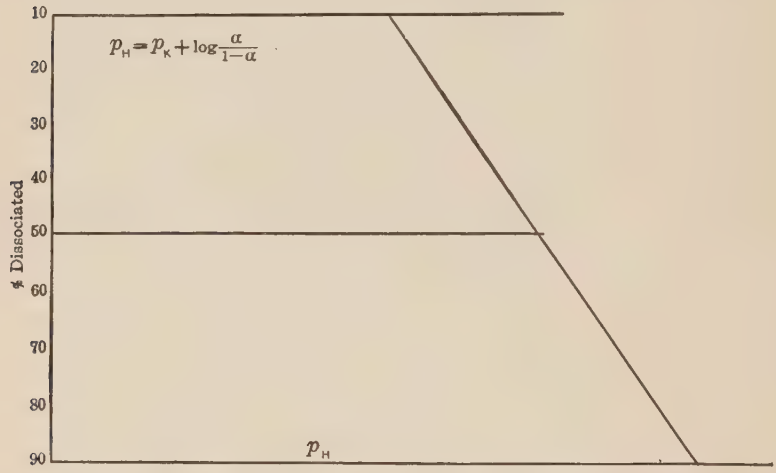


FIG. 12.—Representation of transition interval by straight line (McClendon).

it is equal to the p_H at which 50 per cent of the indicator is present in each of the forms.

J. F. McClendon (3) represents the color change interval (virage) of an indicator by a straight line. From the equation:

$$[H^+] = \frac{[HIn]}{[In^-]}K = \frac{1-\alpha}{\alpha}K,$$

it follows that

$$p_H = p_K + \log \frac{\alpha}{1-\alpha}.$$

The interval (virage) lies between

$$p_H = p_K + 0.95 \quad \text{and} \quad p_K - 0.95.$$

The graph is not a straight line for indicators for which the simple relation does not hold, as is the case with phenol phthalein, salicyl yellow, etc.

Salm (4) has constructed a table in which he gives the color of 70 indicators for all whole-number values of p_H (1, 2, 3, etc.).

INTERVAL OF COLOR CHANGE OF SOME INDICATORS, ACCORDING TO SÖRENSEN

Indicator	Interval in p_H	Amount of Indicator in 10 cc.	Color		Remarks
			Acid	Alkaline	
Methyl violet	0.1– 3.2	3– 8 drops 0.5%	Yellow	Violet	Through green
Methyl green *	0.3– 2	1– 4 drops 0.5%	Yellow	Green-blue	
Tropeolin 00 *	1.3– 3.2	1– 5 drops 1%	Red	Yellow	Sharp
Benzopurpurin *	1.3– 5.0	1– 3 drops 0.5%	Blue-violet	Orange	Notsharp
Methyl yellow (dimethyl-aminoazo benzene)	2.9– 4.0	5–10 drops 0.1%	Red	Yellow	Sharp
Methyl orange	3.1– 4.4	3– 5 drops 0.1%	Red	Orange-yellow	Sharp
Lacmoid	4.4– 6.6		Red	Blue	Sharp
Methyl red	4.2– 6.3	2– 4 drops 0.2%	Red	Yellow	Sharp
p-Nitro phenol	5.0– 7.0	3–20 drops 0.4%	Colorless	Yellow	Sharp
Neutral red	6.8– 8.0	2– 5 drops 0.1%	Red	Yelow	Sharp
Azolitmin	5.0– 8.0	10–20 drops 0.5%	Red	Blue	Fairly sharp
Phenol phthalein	8.2–10.0	3–20 drops 0.5%	Colorless	Red	Sharp
Thymol phthalein	9.3–10.5	3–10 drops 0.4%	Colorless	Blue	Sharp
Alizarine yellow	10.1–11.1	5–10 drops 0.1%	Yellow	Lilac	Sharp
Sodium alizarine sulphonate, 2nd change	10.0–12.0	4–16 drops 0.1%	Brownish-red	Bright yellow	Fairly sharp
Nitramine	10.8–12.8	2– 5 drops 0.1%	Colorless	Orange-brown	Sharp
Tropeolin 0 *	11.0–13.0	5–10 drops 0.1%	Yellow	Orange-brown	Fairly sharp

* These values were determined by the author. The value for methyl red confirms that found by Palitzsch, Biochem. Z. **37**, 131 (1911).

The exact range of color change is therefore not given. S. P. L. Sörensen (5) was the first to determine the interval with great accuracy for a number of indicators. He observed their colors in buffer mixtures whose p_H was determined with the aid of the hydrogen electrode. His results have been used in the construction of Fig. 11, and also in the table, page 59, where data are given for individual indicators that are of practical importance. The author has made some additions to the list. There is an more extensive table at the end of this book, and a chart in which the transition intervals of important indicators are presented graphically as in Fig. 11.

Lubs and Clark (6) found a new series of indicators which show especially beautiful color changes.

According to Clark and Lubs five drops of indicator solution are added to 10 cc. of the fluid to be tested. The following table gives the color change intervals of the Clark and Lubs indicators.

INTERVAL OF COLOR CHANGE OF THE CLARK AND LUBS INDICATORS

Name of Indicator	Trade Name	Concentration	Interval in p_H	Color	
				Acid	Alkaline
p-Xylenol sulphone phthalein (see page 72)	Xylenol blue	0.02%	1.2–2.8	Red	Yellow
Thymol sulphone phthalein	Thymol blue	0.04%	1.2–2.8	Red	Yellow
Tetra bromo phenol sulphone phthalein	Brom phenol blue	0.04%	3.0–4.6	Yellow	Blue
Dibromo orthocresol sulphone phthalein	Brom cresol purple	0.02%	5.2–6.8	Yellow	Purple
Dibromo thymol sulphone phthalein	Brom thymol blue	0.04%	6.0–7.6	Yellow	Blue
Phenol sulphone phthalein	Phenol red	0.02%	6.8–8.4	Yellow	Red
Orthocresolsulphonephthalein	Cresol red	0.02%	7.2–8.8	Yellow	Red
Thymol sulphone phthalein	Thymol blue	0.04%	8.0–9.6	Yellow	Blue
p-Xylenol sulphone phthalein	Xylenol blue	0.02%	8.0–9.6	Yellow	Blue

A. Cohen (7) uses brom xylenol blue (dibromo xylenol sulphone phthalein). It has the same interval as xylenol blue.

Barnett Cohen (8) has extended the Clark and Lubs series by the study of additional indicators which are listed below.

INTERVAL OF COLOR CHANGE OF INDICATORS OF BARNETT COHEN

Name of Indicator	Trade Name	Interval in p_H	Color	
			Acid	Alkaline
m-Cresol sulphone phthalein...	Meta cresol purple	0.5–2.5	Red	Yellow
		7.6–9.2	Yellow	Purple
Dibromo dichloro phenol sulphone phthalein.....	Brom-chlor phenol blue	3.2–4.8	Yellow	Blue
Tetrabromo *m*-cresol sulphone phthalein.....	Brom cresol blue *	4.0–5.6	Yellow	Blue
Dichloro phenol sulphone phthalein.....	Chlor phenol red	5.0–6.0	Yellow	Red
Dibromo phenol sulphone phthalein.....	Brom phenol red	5.4–7.0	Yellow	Red

* The author prefers the name brom cresol blue to that of brom cresol green which B. Cohen suggested.

Michaelis (9) and his coworkers have recently developed a series of one-color indicators, whose use will be more fully described in the fifth chapter.

COLOR CHANGE INTERVAL OF INDICATORS OF MICHAELIS AND GYEMANT

Name of Indicator	Abbreviated Name	Concentration	Interval in p_H	Color	
				Acid	Alkaline
2,4-Dinitrophenol...	α-Dinitrophenol	0.1%	2.0– 4.7	Colorless	Yellow
2,6-Dinitrophenol...	β-Dinitrophenol	0.1%	1.7– 4.4	Colorless	Yellow
2,5-Dinitrophenol...	γ-Dinitrophenol	0.1%	4.0– 6.0	Colorless	Yellow
p-Nitrophenol.....	Dinitrophenol	0.5%	5.0– 7.6	Colorless	Yellow
m-Nitrophenol.....	Dinitrophenol	0.5%	6.5– 8.5	Colorless	Yellow-orange
Alizarine yellow GG	Salicyl yellow	0.1%	10.0–12.0	Pale yellow	Orange

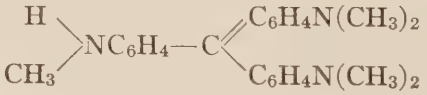
3. The Most Important Properties of Indicators.—A brief description of the most important properties of indicators is given below. (*Cf.* also S. P. L. Sörensen (5).) The author refrains from giving preparation methods, since most indicators may be obtained commercially (from Dr. G. Grübler, Leipzig, for example). The real goal is to give specifications for the identification of the substances, because color compounds are brought into the market under varying names. Many indicators are used as dyes and are therefore described in the table of G. Schultz and F. Julius (Tabellarische Übersicht der künstlichen organischen Farbstoffe, Berlin, 1902). In the following descriptions a number following the name Schultz refers to the corresponding number in the Schultz and Julius table. Where necessary, the method of purifying the trade preparation is given.

Illustrations of the absorption spectra of many indicators are to be found in " Indicators " by E. B. R. Prideaux (10).

(*a*) *The Sörensen Indicators.* (*Cf.* also Table IV at the end of this book.)

Methyl Violet Group

Methyl Violet 6B: Schultz No. 430. Pentamethyl benzyl pararosaniline hydrochloride with varying amounts of the tetra- and hexa-derivatives:

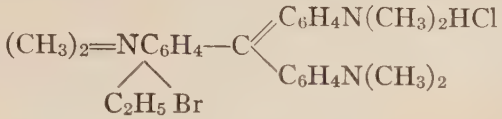


0.1 per cent water solution. Change from yellow to green in interval between p_H 0.1-1.5. Changes from green to violet in interval: p_H 1.5-3.2. From 2–10 drops of indicator per 10 cc. of solution.

Not a very satisfactory indicator; large salt and protein errors; the color changes rapidly.

Methyl Green: Schultz No. 456. Zinc chloride double salt

of the brom-ethylate of hexa- and penta-methyl-monethyl-para-rosaniline:



0.05 per cent aqueous solution. Transition range p_H 0.1–2.3 from yellow to greenish blue. Five drops of indicator per 10 cc. of solution. Large protein and salt errors.

Azo Indicators

Tropeolin 00 (or Orange IV, aniline yellow, or diphenyl orange): Schultz No. 97. Diphenylaminoazo-*p*-benzene sodium sulphonate:

$$SO_3NaC_6H_4N{=}NC_6H_4NHC_6H_5.$$

The commercial preparation is recrystallized from water. A 0.1 per cent aqueous solution is used. Transition range lies between p_H 1.3–3.0; color change is from red to orange yellow; 2 drops of indicator are used per 10 cc. of solution.

It is a suitable indicator; the salt error is small.

Methanil Yellow (or Victoria yellow, Methanil extra, tropeolin G): Schultz No. 91. Sodium salt of *m*-amido benzene sulphonate azo diphenylamine,

$$SO_3NaC_6H_4N{=}NC_6H_4NHC_6H_5.$$

The commercial preparation is recrystallized from water; a 0.1 per cent aqueous solution is used. The color change from red to yellow lies in the range p_H 1.2–2.3. Two drops of indicator are used per 10 cc.

The indicator is satisfactory; it has a small salt error.

Dimethyl amino azo benzene (Methyl yellow, butter yellow):

$$C_6H_5N{=}NC_6H_4N(CH_3)_2.$$

Commercial preparation is recrystallized from dilute alcohol; a 0.1 per cent solution in 90 per cent alcohol is used. Change from red to yellow occurs in range p_H 2.9–4.0. Use 1–4 drops of indicator per 10 cc.

Very satisfactory for titrations, especially of weak bases and of alkali bound to weak acids. Less satisfactory for colorimetric determinations because the indicator rapidly separates out in flocks.

Methyl Orange (helianthin, B, orange III): Schultz No. 96. Dimethylaminoazo benzene sodium sulphonate:

$$SO_3NaC_6H_4N{=}NC_6H_4N(CH_3)_2.$$

Recrystallize the commercial preparation from water. Prepare an 0.1 per cent aqueous solution. The color change from red to orange lies between p_H 3.0–4.4. Use 1–4 drops of indicator per 10 cc. of liquid.

A theoretical study of the behavior of this indicator has been made by Thiel and his coworkers and by Kolthoff (11). According to these investigators, the color change is to be represented by the equation:

$$^{+}HN(CH_3)_2RSO^{-}{}_3 + OH^- \rightleftarrows \underset{\text{yellow}}{N(CH_3)_2RSO_3^-} + H_2O.$$

The red form is the so-called "**Zwitterion,**" or **ampholytic ion** of F. W. Küster (1897). In this case it may be compared with the free amino base of its parent substance, dimethyl amino azo benzene; the red form (ampholytic ion) is comparable to the red cation of the parent substance. The quantitative relations are governed by the law of mass action:

$$\frac{[^{+}HN(CH_3)_2RSO_3^-][OH^-]}{[N(CH_3)_2RSO_3^-]} = \frac{[\text{Red form}][OH^-]}{[\text{Yellow Form}]} = K_B.$$

At 18°, according to the author's experiments, $K_B = 2 \times 10^{-11}$, and $p_K = 10.7$.

Thiel and Dassler (11) found at 25°:

$$K_B = 3.2 \times 10^{-11}; \quad p_K = 10.5.$$

The indicator is very satisfactory for colorimetric determinations; the salt error is small.

Methyl Red: Dimethyl amino azo benzene-o-carboxylic acid:

$$COOHC_6H_4{-}N{=}NC_6H_4N(CH_3)_2.$$

This indicator was introduced by E. Rupp and R. Loose (12). According to Sven Palitzsch (13) the commercial preparation is purified as follows: 4 g. of methyl red are heated with 30 cc. of glacial acetic acid. After filtration, water is added until the solution begins to become turbid. The turbidity is removed by warming and the solution is cooled very rapidly. If the amount of water added was not too large, the methyl red separates in crystals.

An 0.2 per cent solution is used: 1 g. of methyl red is dissolved in 300 cc. of alcohol, and is then diluted with water to 500 cc. The change from red to yellow falls in the range p_H 4.4–6.2. From 1–4 drops of indicator are used per 10 cc.

The indicator is very satisfactory, as the salt error is small.

As in the case of methyl orange, we may regard the free methyl red as an ampholytic ion (Zwitterion). It reacts with acids to form the free carbonylic acid, which in this case is a cation:

$$^{+}HN(CH_3)_2RCOO^- + H^+ \rightleftarrows {}^{+}HN(CH_3)_2RCOOH.$$

The dissociation constant of the acid is:

$$K_a = 2.5 \times 10^{-3}; \quad p_K = 10^{-2.60}.$$

When the methyl red changes from red to yellow we are dealing with its basic properties:

$$\underset{\text{red}}{{}^{+}HN(CH_3)_2RCOO^-} + OH^- \rightleftarrows \underset{\text{yellow}}{N(CH_3)_2RCOO^-} + H_2O.$$

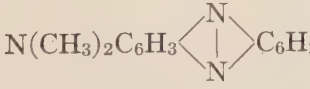
The equilibrium relations are expressed quantitatively by the relation:

$$\frac{[{}^{+}HN(CH_3)_2RCOO^-][OH^-]}{[N(CH_3)_2RCOO^-]} = \frac{[\text{Red form}][OH^-]}{[\text{Yellow form}]} = K_B,$$

$$K_B = 7 \times 10^{-10}; \quad p_K = 10^{-9.15}.$$

(See bibliography under methyl orange.)

Neutral Red: *as*-dimethyl diamino phenazine chloride:



0.1 per cent solution: 0.5 g. of neutral red is dissolved in 300 cc. of alcohol and then diluted to 500 cc. The conversion range red to yellow-orange is p_H 6.8–8,0. From 1–4 drops of indicator are used per 10 cc. of solution. The indicator is satisfactory; salt error is small.

(There is another color change in strongly acid solution; at $p_H = -0.3$ the color is blue; at $p_H = 0$ blue violet; at $p_H = 1$ red.)

Tropeolin 000 (α-naphtholorange): Schultz No. 102. Sulphanilic acid-azo-α-naphthol:

$$SO_3HC_6H_4N{=}NC_{10}H_6OH.$$

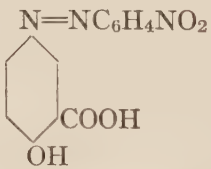
The commercial substance is recrystallized from water; a 0.1 per cent aqueous solution is prepared. Color change brownish yellow to rose red in interval p_H 7.4–8.6. Use 2–5 drops of indicator per 10 cc. of solution.

Curcumine (brilliant yellow S): Schultz No. 100. *p*-Sulphobenzene azo diphenylamine sulphonic acid.

$$SO_3HC_6H_4N{=}NC_6H_3SO_3H(C_6H_5)_2.$$

0.1 per cent aqueous solution. Color change interval lies between p_H 7.4–8.6. Change: yellow to reddish brown. Use 1–5 drops of indicator per 10 cc.

Salicyl Yellow (alizarine yellow): Sodium *p*-nitraniline azo salicylate:



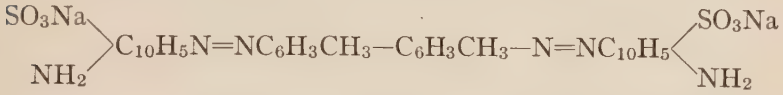
0.1 aqueous solution. Transition from yellow to lilac in range p_H 10.1–12.1. From 1–5 drops of indicator per 10 cc. Very suitable for colorimetric determinations.

Tropeolin 0 (gold yellow): Schultz No. 101. Sodium salt of azo-resorcin sulphanilic acid:

$$SO_3NaC_6H_4N{=}NC_6H_3(OH)_2.$$

Use 0.1 per cent aqueous solution. Changes from yellow to orange brown between p_H 11.0 and 13.0. 1–5 drops of indicator are used per 10 cc. of solution. Nitramine, which has the same range, is a more suitable indicator than tropeolin 0.

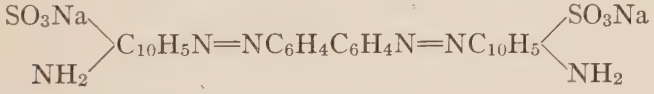
Benzopurpurin 4B (cotton red 4B; Sultan 4B): Schultz No. 268. Sodium salt of *o*-toluidine-diazo-bi-1-naphthylamine-4-sulphonic acid:



The commercial preparation is purified by precipitation from aqueous solution with hydrochloric acid, washing and drying. An amount of alkali insufficient to dissolve the whole precipitate is added and the solution is evaporated. Use 0.1 per cent aqueous solution. The color change from blue violet to red lies in the range p_H 1.3–4. Use 1–3 drops of indicator for 10 cc. of solution.

The salt and protein errors are large and the substance can not be recommended as an indicator.

Congo Red (Congo G. R.): Schultz No. 148. Sodium salt of benzidine disazo-*m*-amidobenzene sulphonic acid-1-naphthylamine-4-sulphonic acid:

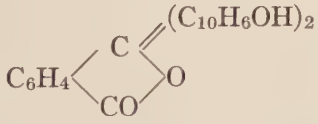


Purification of the commercial preparation is effected as in the case of benzopurpurin. A 0.1 per cent aqueous solution is used. Interval of change between p_H 3.0 and 5.2; color changes from blue-violet to red. 1–3 drops of indicator per 10 cc.

Large salt and protein errors; this indicator can not be recommended.

PHTHALEINS

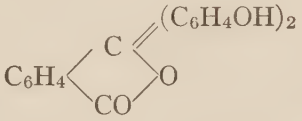
α-Naphthol phthalein:



This substance was first introduced as an indicator by S. P. L. Sörensen and S. Palitzsch (14). They prepared it according to the directions of Grabowski. Melting point 253–255°. The commercial preparation may be purified by washing with alcohol. A 0.1 per cent solution in dilute alcohol is used: 500 mg. are dissolved in 250 cc. alcohol and diluted to 500 cc. Changes from pale yellowish rose to green in range p_H 7.3–8.7. 1–5 drops of indicator are used per 10 cc.

Suitable indicator; salt and protein errors are small.

Phenol phthalein: Melting point 250°.



The commercial preparation is recrystallized from methyl or ethyl alcohol. 1 or 0.1 per cent solution is used. 5 g. or 0.5 g. respectively is dissolved in 300 cc. alcohol, then diluted with water to 500 cc. Changes from colorless to red between p_H 8.2–10.0. Becomes colorless in strongly alkaline solutions just as other phthaleins do.

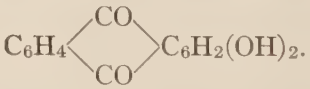
Very suitable indicator; salt and protein errors are small.

Thymol phthalein: Melting point 253°. Use 0.1 per cent solution in alcohol. Changes from colorless to blue in range p_H 9.3–10.5.

Behavior resembles that of phenol phthalein.

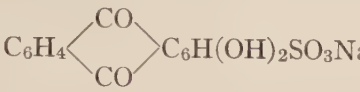
Anthraquinone Derivatives

Alizarine: Schultz No. 523. **α-β-Dioxyanthraquinone:**

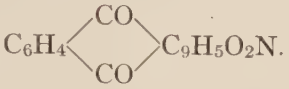


0.2 per cent solution of the trade preparation in 90 per cent alcohol. Changes from yellow to violet in range p_H 5.5–6.8. Use 1–4 drops of indicator per 10 cc. solution.

It is better to use sodium alizarine sulphonate which is soluble in water:



Alizarine Blue: Schultz No. 528. Dioxy-anthraquinone-quinoline. Melting point 270°:

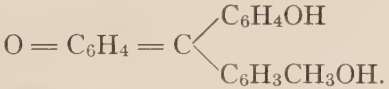


Use saturated solution in alcohol. Changes from yellowish red to blue between p_H 11.0 and 13.0.

Not a very suitable indicator.

Other Indicators

Rosolic Acid (Aurin; yellow Corallin): Schultz No. 457. Mixture of aurin, oxidized aurin, methyl aurin, and pseudo-rosolic acid or corallin phthalein; the latter is the principal component:



Prepare 0.5 per cent solution in dilute alcohol: 2.5 g. of rosolic acid are dissolved in 250 cc. alcohol and diluted with water to 500 cc. Color change red to yellow; range p_H 6.9–8.0. Per 10 cc. solution use 1–3 drops of indictaor.

The indicator is especially suitable for titrations in alcoholic solution.

Isopicramic acid (2, 6-dinitro-4-aminophenol): This indicator was recommended by Meldora and Hale (Chem. World, **1,** 327 (1912). A 0.1 per cent aqueous solution is used. Changes from rose to yellow between p_H 4.1 and 5.6. 1–5 drops of indicator are used per 10 cc. of solution.

Resazurine (Azo Resorcin): 0.1 g. of the dye is dissolved in 20 cc. 0.1 N sodium hydroxide and diluted with water to 500 cc.

The change from orange to dark violet occurs between p_H 3.8 and 6.5. From 1–5 drops of indicator are used per 10 cc.

Lackmoid (or Resorcin blue): $C_{12}H_9O_3N$. Fr. Glaser (15) uses the degree of solubility in boiling water as a criterion of the worth of a commercial preparation. If little or none of the material dissolves in boiling water the preparation is not to be used. If, on the other hand, boiling water is colored a beautiful deep blue the preparation may be used. In this case the alcoholic solution will show a good blue color shading into violet, whereas a less satisfactory quality of lackmoid will dissolve to yield a brownish violet color. The pure blue substance is extracted from the extremely finely powdered commercial preparation with hot water, without carrying the process to completion, in order to avoid the solution of the red fluorescing compound with which such preparations are commonly contaminated. The coloring matter is precipitated from the cold filtered blue solution by making it feebly acid; after several hours the precipitate is collected on a filter and washed thoroughly with cold water. The material is either dried at a low temperature, or dissolved from the paper with alcohol, and the latter is evaporated off on the water bath. The yield is 40 per cent from good commercial preparations. Very pure lackmoid is also obtained by the warm digestion of the commercial material with 96 per cent alcohol, followed by filtration and evaporation over sulphuric acid in vacuo. A 0.2 per cent alcoholic solution is prepared from the purified lackmoid. The change is from red to blue from p_H 4.4 to 6.4. 1–5 drops of indicator are used per 10 cc. of solution.

Hottinger (16) recommends Lackmosol instead of Lackmoid.

Azolitmin (*cf.* F. Glaser (15)): The litmus of commerce has a variable content of azolitmin which averages 5–6 per cent. It is extracted from the litmus by cold water; the solution is evaporated with the addition of sand, after the addition of enough hydrochloric acid to color the liquid strongly red. The dried powder after evaporation is washed on large smooth filters, first with hot, then with cold water, and is then dried completely on the water bath. The azolitmin is thus precipitated on the

sand. In order to prepare a solution, from the powder thus obtained, for use as indicator, the powdered material is extracted on a filter with hot water and several drops of ammonia. The filtrate is acidified with a few drops of of dilute sulphuric acid, is again neutralized and then forms an excellent indicator solution. If the solution is largely diluted and several drops of sulphuric acid are added, the azolitmin separates out almost completely pure as a red-brown precipitate, while a small amount of foreign matter remains in solution. If this purified azolitmin is covered with water which contains traces of ammonia, it dissolves with an uncommonly brilliant blue color. See Glaser (15) for other purification methods. The indicator solution is prepared by dissolving 1 g. of azolitmin in 100 cc. of weakly alkaline water and then neutralizing carefully with acid to the violet color. Change from red to blue lies in range p_H 5.0–8.0. From 1–10 drops indicator per 10 cc.

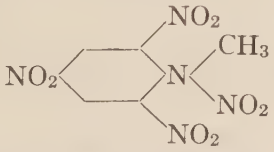
The salt and protein errors are large. The indicator is therefore unsatisfactory for colorimetric determinations.

Di-orthohydroxy-styryl ketone:

$$O{=}C{=}(CH{=}CHC_6H_4OH)_2.$$

This substance was recommended by Aron (17) for use as an indicator. 0.05 per cent solution in alcohol. Changes from yellow to green between p_H 7.3 and 8.7.

Nitramine (Picrylmethylnitramine): 2, 4, 6 trinitro phyenyl methyl nitramine (tetryl or tetralite):



Melting point 127° (van Romburgh (18)) (according to Reverdin 129°; Franchimont 132°).

Picrylmethylnitramine is the first compound which was known as nitramine (van Romburgh (18)). It is obtained by heating dimethyl aniline with fuming nitric acid; it then forms picryl methylnitramine with vigorous evolution of gases:

$$C_6H_5N(CH_3)_2 \rightarrow (NO_2)_3C_6H_2NNO_2CH_3.$$

One of the methyl groups is oxidized and replaced by a NO_2 group during the nitration of the benzene nucleus. An 0.1 per cent solution in dilute alcohol is used (500 mg. in 300 cc. alcohol, then diluted with water to 500 cc.). Changes from colorless to red-brown between p_H 10.8 and 13. One to 10 drops of indicator are used per 10 cc. of solution.

It is a satisfactory indicator; salt error small. The indicator solution should be kept in the dark.

Indicators of Clark and Lubs

The sulphone phthaleins are all indicators with very sharp color change and with colors readily distinguishable from each other; the colors change from yellow to intense red, blue, or purple. Xylene blue (i.e., *p*-xylenol sulphone phthalein) was added to the series by A. Cohen (19). This indicator has the same transition interval as thymol blue, namely between p_H 1.2 and 2.8 (red to yellow) and between p_H 8.0 and 9.6 (yellow to blue). It possesses the advantage of a color intensity twice that of thymol blue. The preparation is analogous to the sulphone phthaleins (*cf.* Clark and Lubs (6)). It is made from a reaction mixture of 10 parts of *o*-sulphobenzene dichloride or the acid anhydride, 10 parts of molten zinc chloride and 15 parts of *p*-xylenol (M. P. 74.5°; B.P. 211 5°); *p*-xylenol may be prepared conveniently from diazotized *p*-xylidine. The reaction mixture thus prepared is heated for six hours in a bath and the melt is then heated with 40 parts of water until it has broken up. The solution is filtered hot and the residue washed with warm water, and finally with a little alcohol. It is then dissolved in an excess of sodium hydroxide and precipitated with hydrochloric acid, stirring well. The precipitate is filtered and recrystallized from alcohol.

The sulphone phthaleins, which are brought on the market by Hynson, Westcott and Dunning, Pharmaceutical Chemists, Baltimore, Md. (and also by Dr. G. Grübler, Leipzig), may be used without further preparation in indicator solutions. The author dissolves 100 mg. of indicator in 20 cc. warm alcohol and

then dilutes with water to 100 cc. Clark first neutralizes the sulphonic acid group, and he gives the following directions: 100 mg. of indicator is rubbed in an agate mortar with the amounts of alkali specified below. When solution is complete the mixture is diluted to 25 cc.

Molecular Weight	Indicator	cc. $\frac{1}{20}$ N NaOH for 100 Mg.
354	Phenol red	5.7
669	Brom phenol blue	3.0
382	Cresol red	5.3
540	Brom cresol purple	3.7
466	Thymol blue	4.3
624	Brom thymol blue	3.2

The following observations should be made about the use of the sulphone phthaleins:

(*a*) The relative change of the color relation between the two forms is greatest in every instance at $p_H = p_{HIn}$, i.e., at the p_H where the indicator has been half transformed. Nevertheless a small change in the ratio of the two colors is more readily perceptible on the acid side of the interval of change than in the region where the indicator has been more than 50 per cent transformed. The reason for this is that the alkaline form of the indicator is much more highly colored than the acid.

(*b*) The color of a sulphone phthalein depends upon the quantity and the intensity of the light that is absorbed. The phenomenon of "dichromatism," that these indicators exhibit, is a factor in the color relations. Brom phenol blue and brom cresol purple, especially, show the phenomenon. They are blue when in thin layers of solution, and purple when seen through greater depths. The explanation of this phenomenon is as follows (*cf.* Clark): In alkaline solution the absorption bands in the yellow and green predominate, and hence the transmitted light is principally red and blue. The incident light has a certain intensity, I. After passage through a unit layer of solution it is Ia, where a is the "transmission coefficient." a depends upon

the nature of the absorbing medium and the wave length of the incident light. After passage through the layer ε the intensity is Ia^{ε}. The intensity of the transmitted blue light is $Ia^{\varepsilon}_{\text{blue}}$, and of the red, $Ia^{\varepsilon}_{\text{red}}$. We will now assume the arbitrary values that Clark used to illustrate the phenomenon. Assume, for example, that the strength (intensity) of the blue light is 100 and that of the red is 30:

$$a_{\text{blue}} = 0.5; \qquad a_{\text{red}} = 0.8.$$

If

$\varepsilon = 1$, $Ia^{\varepsilon}_{\text{blue}} = 50$, and $Ia^{\varepsilon}_{\text{red}} = 24$; Hence blue > red.

For

$\varepsilon = 10$, $Ia^{\varepsilon}_{\text{blue}} = 0.01$, and $Ia^{\varepsilon}_{\text{red}} = 0.30$; Hence blue < red.

If we observe through a thin layer the light is blue, while it appears red through a thicker layer. If the intensities of the incident colors are changed, the color of the transmitted light is also changed. If, for example, $I_{\text{red}} = 100$, and $I_{\text{blue}} = 30$, then for $\varepsilon = 1$, $I_{\text{bl}}a_{\text{blue}} = 15$, $I_{\text{r}}a_{\text{red}} = 80$; hence red > blue. The light is then red. We see therefore that if we bring a solution from daylight (much blue light) into a room that is lighted by a carbon filament lamp the color of the solution changes from blue to red.

These considerations are also important in the explanation of the phenomena which appear in the use of the phenol sulphone phthaleins in turbid solutions, e.g., suspensions of bacterial cultures. When a deep layer of the fluid is viewed, only a small amount of light from the bottom of the vessel reaches the eye. Most of the light enters the side, is reflected by the particles, and has thus traversed a thin layer of liquid. We, therefore perceive a blue color. A comparison of the color with that of the indicator in a clear buffer solution is scarcely possible, for a thin layer of fluid would have to be taken. The result is then only an approximation.

The error may be eliminated by changing the kind of light so that either the red or blue is eliminated. The absorption spectrum of the indicator solution affords a decision as to which color should be avoided.

The author wishes to observe that in various solutions sulphone phthaleins possess colors that are different from those in the buffer solutions which are used for comparison. When the solution to be examined has a " transmission coefficient " for one or both kinds of light absorbed that is different from that of the aqueous buffer solution the colors of the two solutions are no longer comparable. The author has found that the dichromatism of brom phenol blue and other sulphone phthaleins is entirely avoided by various substances, e.g., alcohol, acetone, individual alkaloid solutions. Hence brom phenol blue changes from yellow to pure blue in alcohol or dilute alcoholic solutions; in aqueous solution the intermediate colors are entirely different. These factors must be considered in the colorimetric determination of hydrogen-ion concentration. (See Chapter V.)

Some of the new indicators of Barnett Cohen have distinct advantages. This is especially true of brom cresol blue and chlor phenol red, for they have a pure color change free from dichromatism in the color virage.

The dissociation constants of various indicators are given in Chapter V.

Indicators of Michaelis

These are obtainable from (the plant of Leopold Cassella & Co. in Frankfort a.M.) Dr. G. Grübler, Leipzig, and the United Plants for Laboratory Supplies (Vereinigten Fabriken für Laboratoriumsbedarf) Berlin, N. 39.

The preparation of the indicators is mentioned in the publications of L. Michaelis and A. Gyemant and in those of L. Michaelis and R. Krüger.

Salicyl yellow is *m*-nitrobenzene azo-salicylic acid (alizarine yellow, G. G. Schultz, No. 30).

In contrast with Michaelis, the author uses the indicators in 0.1 per cent alcoholic solution. Only in the cases of *m*-nitrophenol and *p*-nitrophenol are 0.3–0.3 per cent aqueous solution used.

Michaelis and Gyemant (9) give the following directions for testing the suitability of *m*-nitrophenol:

The 0.3 per cent standard solution is diluted five- to tenfold with water. A portion of this diluted solution must remain colorless when a few drops of $\frac{1}{15}$ molar primary potassium phosphate are added (Sörensen); a second portion must become greenish yellow with a few drops of secondary phosphate (Sörensen); a third when treated with a few drops of sodium hydroxide must become visibly darker (brownish) yellow.

4. Classification of Indicators.—As Schoorl (20) has shown, a simple classification of indicators is apparent from the graphical representation of the relationships. If conversion interval lies in the neighborhood of $p_H = 7$ the indicator is equally sensitive toward hydrogen and hydroxyl ions and it is then called *neutral.* If the indicator exponent p_{HIn}—i.e., the negative logarithm of K_{HIn}, which corresponds to the hydrogen-ion concentration when the indicator is 50 per cent changed, is smaller than 7 the indicator begins to change while the reaction is acid; it is then called *alkali sensitive.* If, however, the acid exponent is greater than 7 the change first commences in the alkaline region; the indicator is therefore *acid sensitive.*

Classification of Indicators

Transition interval at about $p_H = 7$; neutral indicator. For example: Neutral red, phenol red, or azolitmin.

Interval at $p_H > 7$: sensitive to acids.

For example: Phenol phthalein and thymol phthalein.

Interval at $p_H < 7$: sensitive to bases.

For example: Methyl yellow, methyl red.

If you treat a neutral solution, as, for example, conductivity water, with various indicators, then it is found that:

Neutral red or phenol red give a transition color.

Phenol phthalein gives the acid color (colorless).

Methyl yellow its alkaline color (yellow).

When the reaction of a solution toward an indicator has been thus established the true reaction of the solution as defined in the first chapter has not been found. If a liquid reacts acid to phenol phthalein we know that its p_H is smaller than 8, and if the reac-

tion toward ethyl yellow is alkaline the p_H is greater than 4.2. Now if we determine the tint that neutral red assumes in a given fluid the alkaline or acid tint corresponds to the true acid or alkaline reaction.

Indicator acids have already been considered. Exactly the same theoretical considerations may be applied to an indicator base, InOH:

$$InOH \rightleftarrows In^+ + OH^-,$$

$$\frac{[In^+]}{[InOH]} = \frac{K_{InOH}}{[OH^-]}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (88)$$

In^+ is the acid and InOH the basic form. Since $[OH^-]$ equals $\frac{K_{H_2O}}{[H^+]}$ the second member of (88) is:

$$\frac{K_{InOH}}{[OH^-]} = \frac{K_{InOH}}{K_{H_2O}} \times [H^+].$$

If the concentration of the alkaline form is placed in the numerator, as was done in the case of acid indicators, we have:

$$\frac{[InOH]}{[In^+]} = \frac{K_{H_2O}}{K_{InOH} \times [H^+]}. \quad . \quad . \quad . \quad . \quad (89)$$

If we substitute for $\frac{K_{H_2O}}{K_{InOH}}$ a new constant K′, equation (89) is thrown into the form:

$$\frac{[InOH]}{[In^+]} = \frac{K'}{[H^+]}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (90)$$

We thus obtain an equation corresponding to that found for acid indicators, and all of the remarks that were there made concerning the transition interval apply also to basic indicators.

The transition interval is different for each indicator, and there is also the limitation that it is not a fixed quantity. Aside from the personal equation, it also varies with the depth of liquid that is observed, with the indicator concentration, and with the temperature.

Formerly the indicator concentration, especially, was not considered thoroughly enough. Since it is significant both in

colorimetric hydrogen-ion concentration determinations, and in many titrations, it will be considered in some detail here.

5. Influence of Indicator Concentration on the Transition Interval.—Obviously there is a fundamental difference between one- and two-colored indicators. The former, being simpler, will be considered first.

(*a*) *One-color Indicators.* We shall again assume that the indicator is an acid of formula HIn; it follows from equation (84) that:

$$\frac{[In^-]}{[HIn]} = \frac{K_{HIn}}{[H^+]},$$

$$[In^-] = \frac{K_{HIn}}{[H^+]}[HIn]. \quad . \quad . \quad . \quad . \quad . \quad . \quad (91)$$

Here $[In^-]$ is the concentration of the colored ion and [HIn] of the colorless. Assume that we have a certain solution whose $[H^+]$ is fixed by a given buffer mixture; then in equation (91) $\frac{K_{HIn}}{[H^+]}$ is a constant which may be called K′; then

$$[In^-] = K' \times [HIn]. \quad . \quad . \quad . \quad . \quad . \quad (92)$$

It is therefore evident that the amount of the colored form is proportional to that of the undissociated indicator. Now if [HIn] increases, then the color will be proportionally deeper for unchanged hydrogen-ion concentration. Since most indicators are only very slightly soluble, [HIn] very soon approaches the saturation value, so that the color can only increase to a limited extent. If the solubility of the indicator is represented by O, then for a fixed hydrogen-ion concentration the maximum color intensity $[In^-]$ is given by:

$$[In^-] = O \times K'. \quad . \quad . \quad . \quad . \quad . \quad . \quad (93)$$

Expressed in words this means that upon addition of a one-color indicator to a buffer mixture the color intensity rises to a maximum at which point the solution is saturated with indicator. On the other hand, a certain minimum indicator concentration is necessary to reach the limit of visibility of the colored form; there must, in other words, be a definite amount of the colored

form present before it can be perceived. This necessary minimum is not invariable for it depends both upon personal equation, and especially upon the depth of liquid used. If it has been found that a certain minimum, which we will call $[In^-_{min.}]$, is necessary to be perceptible, then

$$[In^-_{min.}] = HIn_{min.}] \times K'. \quad . \quad . \quad . \quad . \quad (94)$$

At a given hydrogen-ion concentration the amount of $[In^-]$ i.e., the color intensity, varies between $[HIn_{min.}] \times K'$ and $O \times K'$. The foregoing considerations are of very great significance in the colorimetric determination of hydrogen-ion concentration. We will return to this matter later (Chapter V).

The indicator concentration also influences the magnitude of the transition interval (virage) of a one-color indicator. Suppose that we have two one-color indicators whose colored forms are equally perceptible (hence $[In^-_{min.}]$ the same for both) and whose dissociation constants are also equal, and that an amount of each necessary for saturated solution is always used i.e., ($[HIn] = [O]$), then it follows from equations (91) to (94) that the beginning of the interval lies at hydrogen-ion concentration:

$$[H^+] = \frac{O}{[In^-_{min.}]} \times K_{HIn.} \quad . \quad . \quad . \quad . \quad . \quad (95)$$

If the solubility of one indicator is 100-fold as large as that of the other, then at equal hydrogen-ion concentrations the concentration of the colored form of the first will be one hundred times as large as that of the second. In other words the beginning of the interval of the first indicator will lie at a hydrogen-ion concentration that is one hundred times as large as that of the second indicator, provided we work with saturated solutions. The p_H of the beginning of the interval of the first indicator will be about 2 units smaller than that found when the second indicator is used. Although both indicators have the same dissociation constant, the transition interval of the more soluble one is considerably more extended than that of the second.

The end-point of the interval of the more soluble indicator will be reached only a trifle sooner in case of the more soluble indi-

cator than in that of the less soluble. This difference is of no great significance. At the end of the interval it is difficult to maintain a saturated solution because the indicator salt is readily soluble, and we must therefore add a large amount of indicator.

On the assumption that the end of the interval is reached when 91 per cent of indicator is in the alkaline form, the interval in solution saturated with indicator lies between the hydrogen-ion concentrations:

$$[H^+] = \frac{O}{[In^-_{min.}]} \times K_{HIn}, \quad \text{and} \quad [H^+] = \frac{9}{91} \times K_{HIn} = \frac{1}{10} K_{HIn},$$

or between

$$p_H = p_{HIn} + \log \frac{[In^-_{min.}]}{O} \quad \text{and} \quad p_H = p_{HIn} + 1.$$

It is apparent from the following investigation that these considerations are of practical importance. It has been stated that the solubility of phenol phthalein is considerably greater than that of thymol phthalein, and thus the interval of color change is much greater for phenol phthalein than that of thymol phthalein. Further, the solubility of *p*-nitro phenol is still larger than that of phenol phthalein, so that *p*-nitro phenol has a very great conversion interval.

Phenol Phthalein.—A commercial preparation was purified with methyl alcohol according to McCoy's (21) directions. A 0.1 per cent solution in 70 per cent alcohol was prepared. Various amounts of this solution were allowed to flow into quantities of water in small calibrated flasks so that the final volume was always 50 cc. These solutions were poured into Nessler cylinders and observed against black backgrounds to find the concentration at which opalescence was just barely perceptible. It was found by several repetitions of the experiment that the limit lay at 4 cc. of 0.1 per cent solution in 50 cc. of water; the opalescence was just barely visible. The accuracy of this sort of experimentation is only about 10–15 per cent. According to this experiment the solubility amounts to about 8 cc. of 1 per cent solution in 1000 cc., or about $\frac{1}{4000}$ molar, whereas McCoy found a solubility of $\frac{1}{12000}$ molar.

It was next attempted to find the minimum concentration of the red form $[In^-_{min.}]$ that was just visible against a white background through an 8 cm. depth of liquid contained in a Nessler cylinder. Various dilutions of the 0.1 per cent solution were made. To each 50 cc. was added 1 cc. 4 N sodium hydroxide, and it was then found at what concentration a pale rose color was just perceptible. The color could be seen at an indicator concentration of 2×10^{-6} molar, while at the value 1×10^{-6} molar it was doubtful. Under these conditions we may assume that $[In^-_{min.}]$ is 2×10^{-6} molar. The value is greater than this for ordinary titrations because less favorable conditions of observation then prevail.

The content of colored form which gave no observable change to the eye upon further addition was then determined. The solutions were in Nessler cylinders. This amount was found to be when 5–6 cc. of 0.1 per cent solution were present in 50 cc. and in other experiments 1.5 cc. 0.05 per cent dilution.

It therefore follows that the beginning of the conversion interval of phenol phthalein is at:

$$[H^+] = \frac{O}{[In^-_{min.}]} \times K_{HIn},$$

$$O = \frac{1}{4000} = 2.5 \times 10^{-4} \text{ molar},$$

$$[In^-_{min.}] = 2 \times 10^{-6} \text{ molar},$$

and on the basis of $p_{HIn} = 9.7$,

$$p_H = 9.7 + \log \frac{2 \times 10^{-6}}{2.5 \times 10^{-4}} = \mathbf{7.6}.$$

As a matter of fact a boric acid-borax mixture saturated with phenol phthalein shows a barely visible rose color at $p_H = 7.8$.

When McCoy stated that the rose coloration due to phenol phthalein is first visible at $[H^+] = 10^{-8}$ he should also have stated the concentration of indicator that he used.

The end-point of the interval lies at a p_H that is smaller than 10 in our instance, and for saturated solution of phenol phthalein at $p_H = 9.4$. This indicates, therefore, that p_{HIn} not constant.

Thymol Phthalein. The investigation was conducted in the manner that has been described, so that it will suffice here to give the results without the details.

The solubility is much smaller than that of phenol phthalein, since a turbidity appears when 12.5 cc. of a 0.1 per cent solution are present per liter, i.e., for 1.25×10^{-6} g. per liter.

Further, we have:

$$[In^-_{min.}] = 1 \times 10^{-6} \text{ g. per liter.}$$

The beginning of the transition interval is at:

$$p_H = p_{HIn} + \log \frac{1 \times 10^{-6}}{1.25 \times 10^{-6}}.$$

The start of the interval therefore lies at a p_H which is about of the same magnitude as p_{HIn}. According to Sörensen the interval of thymol phthalein lies between p_H 9.3 and 10.5. The author found the beginning at $p_H = 9.2$. From other experiments he found that the value for p_{HIn} is not $\frac{9.3 + 10.5}{2} = 9.9$, but only equal to 9.2.

It is therefore evident that p_{HIn} can not always be read directly from the curve (see page 57) as the point at which 50 per cent of the indicator has gone over to the alkaline form (*cf.* Rosenstein, 1912). Since this point has a special significance we may better call this p_H the *indicator exponent*, p_I.

Para Nitro Phenol. The solubility in this case plays an especially important rôle for the interval. A 1 per cent solution was made from a preparation of melting-point 112–113°; more dilute solutions were prepared from the 1 per cent solution. Upon observing the yellow color in Nessler cylinders the author found:

$$[In^-_{min.}] = 10^{-7} \text{ molar.}$$

$[In_{max.}]$ is naturally much more difficult to determine. The alkaline color of *p*-nitro phenol is greenish yellow at small concentrations, golden yellow at larger concentrations. When 1 cc. of 1 per cent *p*-nitro phenol was added to 50 cc. of a very dilute alkali solution further addition of the indicator gave almost no

perceptible change. $[In^-_{max.}]$ is therefore about 2×10^{-4} g. per liter. From the investigations of Sörensen (see table, page 59) the interval of *p*-nitro phenol is found to be between p_H 5.0 and 7.0. Therefore the dissociation constant of the indicator is deduced to be 10^{-6}.

Since *p*-nitro phenol is a very readily soluble indicator, it is to be expected that it should be able to impart a yellow color to the solution at a much lower hydrogen-ion concentration when a large quantity of it is used. This is shown to be true from the following tests with 0.1 N acetic acid which has a p_H of 2.87.

10 cc. plus 1 cc. of 1 per cent *p*-nitro phenol; pale blue color;
10 cc. plus 2 cc. of 1 per cent *p*-nitro phenol; only slight yellowish. blue coloration;
10 cc. plus 3 cc. of 1 per cent *p*-nitro phenol; plain yellow color.

With $\frac{1}{15}$ molar NaH_2PO_4.

Enough 0.1 per cent *p*-nitro phenol solution was added to 10 cc. of aqueous solution to give a slight visible yellow coloration.

Upon addition of 1.7–1.8 cc. the color was extremely pale, but was plainly perceptible when 2.0 cc. had been added. The experiment was repeated, using 1 per cent solution. Upon addition of

0.14 cc. of 1 per cent solution no color evident,
0.18 cc. of 1 per cent solution pale yellowish shade,
0.20 cc. of 1 per cent solution color quite plain.

It is to be concluded therefore that *p*-nitro phenol may change even at p_H = about 3.0 (i.e., in about 0.1 N acetic acid) if a sufficient amount of indicator is present.

The approximate value of the dissociation constant may be calculated from these data. Having established that a pale yellow color appears in 0.1 N acetic acid when 2 cc. of 1 per cent solution have been added to 10 cc. and that $[In^-_{min.}]$ is about equal to 10^{-7} molar, we find:[1]

$$\frac{[In^-]}{[HIn]} = \frac{139 \times 10^{-7}}{2} = \frac{K_{HIn}}{[H^+]} = \frac{K_{HIn}}{10^{-3}},$$

$$K_{HIn} = \text{about } 7 \times 10^{-9}.$$

[1] The molecular weight of *p*-nitro phenol is 139.

We see therefore that an erroneous value is found for the dissociation constant of *p*-nitro phenol if we set the value of p_{HIn} equal to p_H at the middle of the conversion interval as given in Sörensen's table (*cf.* also Chapter V, page 162).

No further emphasis is needed to show that these deductions and considerations are of great significance for the colorimetric determination of hydrogen-ion concentration. The concentration error would be largest in using *p*-nitro phenol as indicator, less in the case of phenol phthalein, and smallest when using the difficultly soluble thymol phthalein.

(*b*) *Two-color Indicators.* In this case the influence of concentration upon the conversion interval is much more involved than in the former class of indicators. It should be observed at the outset that the two branches of the transition curve (Fig. 11 page 57) are not in general symmetrical with respect to each other because the sensitivity with which the acid form is perceptible in presence of the alkaline is generally different from that in the reverse case. For example, the red acid form of methyl yellow has a much greater color intensity than the alkaline form, the concentrations being equal, so that the former may be detected in presence of the latter at a much lower concentration than in the reverse case. We will deal with this question more extensively later.

A further difficulty arises when one of the two forms is difficultly soluble. This point has to be watched for, especially in colorimetric hydrogen-ion concentration determinations.

As an example may be cited the azo-type of dyes, as for instance dimethylaminoazobenzene (methyl yellow).

Methyl yellow is a weak base, of $p_{BOH} = 10$, that is very difficultly soluble and shows a yellow color. The red-colored salt, on the other hand, dissolves more readily in water. In equation (90):

$$\frac{[InOH]}{[In^-]} = \frac{K'}{[H^+]} \quad \ldots\ldots\ldots \quad (90)$$

[InOH] is the concentration of the yellow form, [In^-] that of the red form. For every given hydrogen-ion concentration there is a definite relation between the yellow and the red form. As we

add increasing amounts of indicator to a given solution the magnitudes of [InOH] and [In^-] will increase equally until the solution is saturated with InOH. From this point on [InOH] and [In^-] remain constant. The excess of indicator remains in solution in a colloidal form that possesses the same yellow color as the alkaline form. In such a solution the color of the indicator corresponds to a stronger alkaline reaction than is actually at hand.

For the above reasons it is more advisable to use methyl orange, which is readily soluble in both acid and alkaline solution, in colorimetric determinations, rather than methyl yellow.

Methyl Yellow or Dimethylaminoazobenzene. A preparation purified by boiling a number of times with fresh portions of water was used for the preparation of saturated solutions.

1. One portion was thoroughly shaken with water.

2. Another part was boiled with water and allowed to stand for several days.

3. Finally an alcoholic solution was added to water and allowed to stand for several days. The clear solution was siphoned off carefully in each case and compared colorimetrically with dimethyl yellow solutions of known concentration. Well agreeing values were found, indicating a solubility of about 0.5 mg. per liter. Hence if a 0.1 per cent solution is used to make a colorimetric determination of [H^+] in 10 cc. of a fluid not more than 0.05 cc., or about one drop, should be used.

The sensitivity of the detection of one form in the presence of the other will be considered in the next chapter.

6. Effect of Temperature on the Transition Interval of Indicators.—Schoorl (20) has dealt with the effect of heat upon indicators. He found that on boiling the color of the alkali-sensitive indicators is displaced toward the basic side, and that of the acid-sensitive indicators toward the acid side. He found an explanation in the increasing dissociation constant of water. This interpretation clarifies the discussion.

The color of an acid indicator of acidic nature is governed by the equation:

$$\frac{[In^-]}{[HIn]} = \frac{K_{HIn}}{[H^+]}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (85)$$

If an acid-sensitive indicator begins to change at a hydrogen-ion concentration of 10^{-10} this corresponds to a hydroxyl-ion concentration of 10^{-4} at room temperature. Upon warming, the hydroxyl-ion concentration which was already $\frac{1}{10000}$ N is hardly changed, remaining of order of magnitude 10^{-4}. Since the dissociation constant of water at 100° is about 100 times greater than at 18°, the hydrogen-ion concentration will also be 100 times as great because $[H^+] = \frac{K_{H_2O}}{[OH^-]}$. The degree of dissociation of acids and bases is in general little changed with change in temperature. On the assumption that it remains constant for the indicator it follows from equation (85) that: $\frac{[In^-]}{[HIn]}$ at 100° is 100 times smaller than at 18° because $[H^+]$ has become 100 times larger. There is therefore too little of the alkaline form present to make a color change perceptible. At boiling temperature enough alkali must be added to make $[H^+]$ again 100 times smaller, thus approximating the amount at room temperature. This, in turn, involves a strong increase in hydroxyl-ion concentration so that the relation $\frac{[OH^-]}{[H^+]}$ at the beginning of the change interval is much greater at 100° than at room temperature.

If we now consider a basic indicator, then according to equations (89) and (90):

$$\frac{[InOH]}{[In^+]} = \frac{K'}{[H^+]} = \frac{K_{H_2O}}{K_{InOH}} \times \frac{1}{[H^+]}.$$

If the beginning of the change of such an indicator lies at $[H^+] = 10^{-4}$, i.e., $\frac{1}{10000}$ N, at room temperature, then this $[H^+]$ will be practically unchanged by the increasing dissociation of water upon heating to boiling. On the other hand, K_{H_2O} increases 100 fold, while K_{InOH} is assumed to remain unchanged. The second member of the equation derived (89) and (90) is thus 100 times larger. The indicator will just begin to change when enough acid is present to make $[H^+]$ 100 times greater. The beginning of the change at higher temperature thus lies at much smaller p_H but at unchanged p_{OH}.

It follows also from consideration of hydrolysis that acid indicators on warming change their color toward the acid side, and basic ones toward the basic side. If BIn is an indicator salt then the hydrolysis in aqueous solution is represented by the equation:

$$In^- + H_2O \rightleftarrows HIn + OH^-,$$

$$\frac{[HIn][OH^-]}{[In^-]} = \frac{K_{H_2O}}{K_{HIn}}.$$

If upon boiling K_{H_2O} becomes 100 times larger[2] and if K_{HIn} remains constant then $\frac{[HIn]}{[In^-]}$ becomes 100 times larger since the other terms are unchanged. There is therefore formed a 100 times larger amount of the acid form.

In the following experiments it will be shown whether the change interval of acid-sensitive indicators is actually displaced about 2 units along the p_{OH}-axis, and for alkali-sensitive forms 2 units along the p_H-axis. When this is the case it proves that the dissociation constants of the indicators do not change upon heating.

Nitramine: This indicator does not change its sensitivity toward alkalies and hence for hydroxyl ions at higher temperatures. It follows therefore that nitramine acts as a basic indicator.

Thymol Phthalein: 250 cc. of distilled water were placed in a much-used well-steamed-out Erlenmeyer flask of Jena glass and 10 drops of 0.1 per cent thymol phthalein solution were added. 0.1 N sodium hydroxide was added until a pale blue color was established at boiling temperature. 0.7–0.8 cc. was required. The color intensity was at a maximum after the addition of 5 cc. 0.1 N alkali. The indicator begins to change at a concentration of 3 cc. of 0.1 N alkali per liter, i.e., at $[OH^-] = 3 \times 10^{-4}$ and $p_{OH} = 3.53$. Since p_{H_2O} at 100° is 12.2, the indicator begins to change at $p_H = 12.2 - 3.53 = 8.67$.

[2] According to the investigations of Kohlrausch and Heydweiller: Ann. d. Physik (4) **28**, 512 (1909), p_{H_2O} is 12.24 at 100°; Lorenz and Böhi: Z. phyzik. Chem. **66**, 733 (1909) found 12.13. We may assume p_{H_2O} to have the average value 12.2 at 100°.

The change is complete at $[OH^-] = 2 \times 10^{-3}$, and $p_{OH} = 2.70$, i.e., at $p_H = 9.50$.

At 100°, therefore, the indicator changes at a point where the ratio $OH^- : H^+$ is much larger than at 18°. As has been stated, Schoorl had pointed out this fact.

It is striking that the indicator begins to change at a smaller p_H at 100° than at room temperature. This does not necessarily indicate an increase in the dissociation constant of thymol phthalein, but may be occasioned by the greater solubility of the indicator at higher temperature. As has been explained, solubility plays an especially important rôle in the conversion interval of thymol phthalein. It is evident that 10 drops of 0.1 per cent thymol phthalein solution would not dissolve at room temperature, but would do so at the boiling point. It is therefore probable that the fact that the change begins at a smaller p_H at 100° than at room temperature is to be ascribed partly to the greater solubility, and hence concentration, at the higher temperature.

Phenol Phthalein: Similar experiments to those above described were performed. In the presence of 5 drops of 1 per cent phenol phthalein solution per 250 cc. of boiling water a pale rose color appeared upon the addition of about 0.20 or 0.21 cc. 0.1 NaOH. Hence $[OH^-]$ is 8×10^{-5}, p_{OH} 4.1, and $p_H = 8.1$.

The color intensity was at a maximum after the addition of 1.5 cc. 0.1 N NaOH to 250 cc. $p_{OH} = 3.21$ and p_H about 9.

The change of the indicator therefore begins at practically the same p_H but at a much smaller p_{OH} than at room temperature. This conclusion was tested by boiling an 0.2 N sodium acetate solution (Kahlbaum preparation) after addition of phenol phthalein. Such a solution reacts very feebly alkaline to the indicator at room temperature. As previously mentioned, the dissociation constant of acetic acid, according to Noyes (21), changes but little upon heating. (K_{HAc} is 18.2×10^{-6}, and 11.1×10^{-6} at 100° C.) The decrease in the dissociation is therefore so small that it can occasion only a small increase in the degree of hydrolysis. K_{H_2O} increases one hundred-

fold, thus strongly increasing the hydrolysis, decreasing p_{OH} by about one unit, and p_H only very slightly. If these considerations are true the color of the boiling solution will be only little more strongly basic than at room temperature.

This was found to be the case. The solution became a more pronounced rose color on boiling. Upon cooling the solution it was found that this phenomenon did not arise from extraction of alkali from the glass, or from the formation and vaporization of acetic acid. (It was a striking fact that the cooled solution, although at first pale rose colored, became colorless, even when the air entered the vessel through a soda-lime tube. Thus far no explanation has been found for this phenomenon, which was shown by solutions of a number of different preparations.)

Thymol Blue: 250 cc. of water required 2.5 cc. of 0.01 N NaOH at 100° before the liquid showed a greenish shade: $[OH^-] = 10^{-4}$, $p_{OH} = 4.0$ and $p_H = 8.2$. The indicator therefore behaves almost exactly in the same way as phenol phthalein. The maximum color intensity appeared after the addition of about 1.5 cc. of 0.1 N NaOH, $p_{OH} = 3.2$, $p_H = 9.0$.

Cresol Red: 250 cc. of water required 0.6 cc. 0.01 N NaOH before a pale rose color could be seen: $[OH^-] = 2.4 \times 10^{-5}$, $p_{OH} = 4.6$, $p_H = 7.6$. The indicator begins to change at $p_H = 7.2$ at room temperature.

Phenol Red: 0.35 cc. of 0.01 N NaOH was required to produce a pale rose color in 250 cc. of water at 100°: $[OH^-] = 1.2 \times 10^{-5}$, $p_{OH} = 4.9$, and $p_H = 7.3$. At room temperature the change begins at $p_H = 6.8$.

As a result of the experiments it was found in each case that the dissociation constants of the phthaleins and sulphone phthaleins are little altered upon heating to boiling.

Methyl Red: The color of this indicator changes only a little toward the alkaline side upon heating to boiling. Methyl red acts both as a weak base and as a weak acid so that heating increases both the hydrolysis of salts formed from the acid and the base. Since, however, the dissociation constant of the basic part is much smaller than that of the acidic, and since the solutions of the indicator contain much of the salt of the acidic

part together with undissociated methyl red in the transition range, the color is displaced somewhat toward the alkaline side upon boiling. This was made evident in the following experiments.

A very dilute solution of acetic acid in boiled water was treated with a little methyl red, and divided into two portions. One half was heated and compared with the cold portion. The heating had produced an alkaline shade. Analogous experiments were made with boric acid solutions which did not give as clear a picture of the color displacement, and with hydrochloric acid solutions which showed the same phenomena as the acetic acid solutions.

By way of further confirmation, the color change of methyl red in boiling ammonium chloride solution was observed. According to the data of Noyes (8, Chapter I) the dissociation constant of ammonia is unchanged on heating. Since K_{H_2O} becomes one hundred-fold larger upon boiling, p_H must become somewhat smaller and the color of the solution should be displaced toward the acid side. This was also confirmed by experiment: A 0.2 N ammonium chloride solution, treated with a few drops of methyl red, had a transition color ($p_H = 5.1$). Upon boiling the color became redder, but not as intense as the color at $p_H = 4.2$. Upon cooling the p_H went back to the original value.

It may be concluded from these consistent experiments that the range of color change, expressed in p_H values, remains almost the same at boiling temperature as at room temperature.

p-Nitro Phenol: Upon boiling the color shade is displaced but slightly toward the basic side. This does not correspond to our expectation of the behavior of an acid indicator, unless it is assumed that the dissociation constant of the indicator increases with rise in temperature. This is, in fact, the case.

Hantzsch found that the color of a solution of *p*-nitro phenol in organic solvents became darker on warming. This was also found to be true for aqueous solutions in the following experiments.

A strongly alkaline solution, that contained so little *p*-nitro phenol that it appeared bright yellow when cold, became darker

yellow on heating, and upon cooling returned to its original shade.

The change in color of *p*-nitro phenol on heating was also evident in the following experiment.

A boric acid solution colored yellow by *p*-nitro phenol became greenish yellow on heating. Upon cooling the original color returned.

It is clear from all of these experiments that the interval of *p*-nitro phenol is but slightly displaced by heating. It may be deduced by extrapolation from the work of L. Michaelis and A. Gyemant (9) that the constant of *p*-nitro phenol is about tenfold greater at 100° than at room temperature.

Methyl Yellow: 250 cc. of distilled water with 5 drops of 0.2 per cent dimethyl yellow solution were heated to boiling in a Jena flask and then titrated with 0.1 N hydrochloric acid until the color was perceptibly different from that of a duplicate solution. This occurred when 0.8–0.9 cc. 0.1 N HCl had been added, corresponding to: $[H^+] = 3.4 \times 10^{-4}$, $p_H = 3.47$ and $p_{OH} = 8.73$. After the addition of 12.5 cc. 0.1 N HCl the full acid color was attained, i.e., at $[H^+] = 5 \times 10^{-3}$, $p_H = 2.30$, $p_{OH} = 9.90$.

If the dissociation constant of methyl yellow had remained unchanged on heating, the change at the boiling point would have occurred at a p_H two units smaller than at 18°, hence at a p_H = about 2.0. The fact that the change starts at $p_H = 3.47$ points to a marked increase in the dissociation constant of dimethylaminoazobenzene on boiling.

A. Richter (23) gives the following figures for the indicator exponent of methyl yellow at various temperatures:

Temperature	p_K
20°	10.91
40°	10.47
60°	10.15
75°	9.92

These values are in close agreement with the author's data.

Methyl Orange: Sodium dimethylaminoazobenzene sulphonate was studied in the same manner as methyl yellow. The change began upon the addition of 0.5–0.6 cc. 0.1 N HCl: $[H^+] = 2.2 \times 10^{-4}$, p_H 3.66 and p_{OH} 9.64. In this instance also the dissociation constant of the base increases on boiling (*cf.* also Tizard (24)).

Thymol Blue: 100 cc. of water required 2.5 cc. 0.1 N HCl before the yellow liquid became slightly rose colored: $[H^+] = 2.5 \times 10^{-3}$, $p_H = 2.6$ and $p_{OH} = 9.6$. At 100° the change began at about the same p_H as at room temperature ($p_H = 2.8$).

Tropeolin 00: 45 cc. of water containing 3 drops of 0.1 per cent tropeolin solution were boiled and titrated with 0.1 N hydrochloric acid. The start of the change was after addition of about 5 cc. of the acid: $[H^+] = 10^{-2}$, $p_H = 2$ and $p_{OH} = 10.2$. The end of the interval is very difficult to observe in this case.

The dissociation of tropeolin 00 also increases on heating since the beginning of the change is at p_H 3.1 at room temperature.

Methyl Violet: 250 cc. of water were boiled after the addition of methyl violet, and titrated with 0.5–4 N hydrochloric acid. The blue color began to appear after addition of 10 cc. of 0.5 N HCl, or 0.4 cc. 4 N HCl: $[H^+] = 1.8$ to 2×10^{-2}, $p_H = 1.70$ and $p_{OH} = 10.50$. The very difficultly perceptible end of the change was determined with 4 N hydrochloric acid. It appeared to let at about 0.5 N solution where the color is yellow.

It appears from all of these experiments that the position of the color change interval of most indicators is appreciably changed by heating. The sulphone phthaleins alone have almost unchanged sensitivity for hydrogen ions as the temperature is changed. In the following table the values have been summarized.

7. Influence of Alcohol on the Sensitivity of Indicators.— Almost nothing is known about the influence of various solvents upon the sensitivity of indicators. Various investigators, to be sure, have made qualitative experiments on the direction toward which the conversion interval of certain indicators is displaced by the addition of methyl and ethyl alcohol, but quantitative data are still lacking. If one reads the review that A. Thiel (28)

ALTERATION IN COLOR-CHANGE INTERVAL OF INDICATORS ON HEATING

(p_{H_2O} at 18° = 14.2, at 100° 12.2)

Indicator	18°		100°	
	p_H	p_{OH}	p_H	p_{OH}
Methyl violet	0.1– 3.2	14.1–11.0	0.5– 1.7	11.7–10.5
Thymol sulphone phthalein	1.2– 2.8	13.0–11.4	1.2– 2.6	11.0– 9.6
Tropeolin 00	1.3– 3.3	12.9–10.9	0.8– 2.2	11.2–10.0
Methyl yellow	2.9– 4.0	11.3–10.2	2.3– 3.5	9.9– 8.7
Methyl orange	3.1– 4.4	11.1– 9.8	2.5– 3.7	9.7– 8.5
Methyl red	4.2– 6.3	10.0– 7.9	4.0– 6.0	8.2– 6.2
p-Nitro phenol	5.0– 7.0	9.2– 7.2	5.0– 6.5	7.2– 5.7
Phenol sulphone phthalein	6.8– 8.4	7.4– 5.8	7.3– 8.3	4.9– 3.9
o-Cresol sulphone phthalein	7.2– 8.8	7.0– 5.4	7.6– 8.8	4.6– 3.4
Phenol phthalein	8.3–10.0	6.2– 4.6	8.1– 9.0	4.1– 3.2
Thymol sulphone phthalein	8.0– 9.6	6.2– 4.6	8.2– 9.2	4.0– 3.0
Thymol phthalein	9.3–10.5	4 9– 3.7	8.7– 9.5	3.5– 2.7
Nitramin	11.0–12.5	3.2– 1.7	9.0–10.5	3.2– 1.7

gives in his book entitled " Der Stand der Indicatorenfrage," the impression received is that the whole subject is still in a very confused state. Waddell (28) has already investigated the influence of various weakly-ionizing solvents, namely alcohol, acetone, ether, chloroform, and benzene, upon the color of the following indicators: Fluorescine, corallin, phenacetolin, cyanine, *p*-nitro phenol, phenol phthalein, methyl orange, lacmoid, and curcumin; his purpose was to test the correctness of the Ostwald theory of indicators. Scholtz (28) described some qualitative experiments of which the following is of interest here: If alcohol is added to a feebly alkaline aqueous phenol phthalein solution, the rose color vanishes. Upon warming the solution the rose color reappears. Cohn (28) confirmed this experiment of Scholtz, and among other things established the fact that a neutral alcoholic soap solution does not color phenol phthalein in the cold, but does at a higher temperature (*cf.* also Braun (28) and F. Goldschmidt (28), R. Meyer and O. Spengler (28) O. Schmatolla (28)). R. Hirsch (28) found that methyl alcohol has about a tenfold stronger

effect that ethyl alcohol in depressing the color of weakly alkaline aqueous phenol phthalein solutions. McCoy (28) employed a $\frac{1}{20000}$ N baryta solution that contained an equivalent amount of phenol phthalein. When he added 2 cc. of alcohol to 100 cc. of this solution, the color was reduced to about half of its original intensity; 0.4 cc. of alcohol had a still plainly perceptible action. Apparently we can not attribute too much significance to these data of McCoy because he apparently had at this great dilution a solution of barium carbonate rather than hydroxide. Alcohol has an appreciable effect on the degree of hydrolysis of the carbonate. According to J. H. Hildebrand (28) alcohol exerts a much greater influence on phenol phthalein than upon some of the other indicators that he investigated. His principal conclusions are assembled in the following table:

INFLUENCE OF ALCOHOL ON INDICATORS ACCORDING TO HILDEBRAND

Indicator	Per Cent Dissociated		Per Cent Decrease in in Color
	Without Alcohol	With 13% Alcohol	
Phenol phthalein	67	30	37
Litmus	76	80	— 4
Rosolic acid	57	57	0
p-Nitro phenol	80	81	— 1

It should be noted that Hildebrand conducted his experiments on the influence of alcohol upon phenol phthalein with a dilute ammonia solution, and did not take into account the fact that the degree of dissociation of ammonia is reduced by alcohol.

An imporant investigation of titration in ethyl alcohol as a solvent was recently published by E. R. Bishop, E. B. Kittredge, and J. H. Hildebrand (28). They determined the titration curves of various acids and bases in ethyl alcohol solution with the aid of the hydrogen electrode. They observed as well between what electromotive force limits, of the cell employed, the color-change intervals of various indicators lay. Unfor-

tunately the constant of the hydrogen electrode in alcoholic solution is unknown, so that it is impossible to deduce the interval in p_H from their data.

Because of the fact that there is still little information about the influence of alcohol on the sensitivity of indicators, the author (27) has made an extended investigation. It should be noted that not nearly enough data are at hand as a result of this work, and that many experiments in other directions must be made. Some of the findings of the work are of theoretical and practical interest, and will therefore be given here. The first series of tables, especially, has a practical significance because the sensibility of the indicators for acid or alkali in alcoholic solutions of various concentrations can be easily read off.

The experiments were made by adding indicator to a definite amount of water-alcohol mixture and then adding acid or alkali until the color was perceptibly different from the color imparted to water. The alcoholic content is expressed in volume per cent.

Thymol Phthalein		Phenol Phthalein	
Alcohol, Per Cent	Sensitivity for Alkali	Alcohol, Per Cent	Sensitivity for Alkali
0	0.002 N	0	0.0002 N
17	.004 N	17	.0004 N
20	.0065 N	28	.0008 N
48	.012 N	48	.0013 N
80	.025 N	80	.0015 N
96	.032 N	96	.002 N

It is plainly to be seen that the numbers of these tables have only practical significance, because the actual sensitivity of thymol and phenol phthalein is much greater toward alkali than there indicated. Higher accuracy could be attained only with buffer solutions. It should be remarked that alcohol changes not only the intensity of the color of phenol phthalein, but also the quality of the color. Phenol phthalein is cherry-red in alkaline aqueous solution, more violet in dilute alcoholic solu-

tion, and bluish violet in concentrated alcoholic solution. Besides, the full alkaline color of phenol phthalein is much less intense in alcohol than in water.

Experiments were made using methyl alcohol instead of ethyl. As was to be expected, it was found that the influence of methyl alcohol is smaller than that of ethyl.

The sensitivity of the neutral indicators, which have a change interval in the region of $p_H = 7$ in water, can not be determined in the above fashion because traces of impurities in water have too much influence on the result. It is therefore necessary to use buffer mixtures. Since the hydrogen exponents of such mixtures in alcoholic solution are at present unknown, exact experiments could not be carried out.

Nevertheless the following experiments have practical significance because it may be deduced from the results which indicators have a sharp change in concentrated alcoholic solution.

α-Naphthol Phthalein: Change in water lies between p_H 7.3 and 8.7 (rose to blue). Fifteen drops of 0.2 per cent α-naphthol phthalein were added to 25 cc. 96 per cent alcohol, then 0.01 N alkali was added and the color determined in Nessler colorimeter glasses:

α-Naphthol Phthalein in 96 Per Cent Alcohol

Cc. of 0.01 N Alkali Added	Color of the Solution
.0	bright brown
0.2	change toward yellow
0.4	pure yellow
0.4–0.7	straw yellow
0.8	yellowish green
1.0	green
much alkali	blue

The bi-basic character of α-naphthol phthalein accounts for its characteristic behavior in alcohol.

Rosolic Acid: Changes in water between p_H 6.9 and 8.0 (yellow to red). The indicator is pure yellow in alcohol of 96 and 99.7 per cent strength. The color is rose red after the addition of 0.1 cc. of 0.01 N sodium hydroxide to 50 cc. The color is at

a maximum when 0.2 to 0.3 cc. of 0.01 N alkali is present per 50 cc. The change in alcohol is therefore very sharp.

Phenol Sulphone Phthalein: Change in water between p_H 6.8 and 8.0. Behaves like rosolic acid in alcoholic solution.

Neutral Red: Change in water lies between p_H 6.8 and 8.0. The indicator is yellow (alkaline color) in 99.7 per cent alcohol in contrast with the two preceding indicators. 25 cc. of 99.7 per cent alcohol with a little of the indicator are reddened by 0.1 cc. of 0.01 N acid; the intensity is at a maximum when 0.25 cc. of the acid is present per 25 cc. The change in alcohol is therefore very sharp.

Azolitmin: Conversion interval in water between $p_H = 5.0$ and 8.0 (red to blue). In alcohol of 99.7 or 96 per cent strength the indicator has its transition color, namely violet. The color change with acid or alkali is not sharp. Azolitmin is therefore an unsatisfactory indicator in alcoholic solution.

Curcumine: Aqueous solution change lies between p_H 7.8 and 8.2. It changes with about the same amount of alkali in alcohol as in water.

Lackmoid: Change in water lies between p_H 4.4 and 6.4 (red to blue). It has the alkaline color (blue) in 99.7 and 96 per cent alcohol. 0.15 cc. 0.01 acid colors the indicator rose red in 25 cc. of 96 per cent alcohol. Sharp change.

Brom Cresol Purple: Change in water is between p_H 5.2 and 6.8 (yellow to purple). The color is greenish yellow in 99.7 per cent alcohol. 25 cc. of alcohol with 0.1 cc. 0.01 N hydrochloric acid colors the indicator pure yellow; conversely, with 0.1 cc. 0.01 N alkali it is bluish green, and with 0.2 cc. blue. Sharp change.

p-Nitro Phenol: Behaves the same in alcoholic solution as in water.

Sodium Alizarine Sulphonate: Change in water lies between p_H 3.7 and 5.2 (yellow to violet). The color is brown in 99.7 per cent alcohol. With alkali it becomes red-brown, not violet as in water.

Methyl Red: Transition interval in water: p_H 4.2 to 6.3 (red to yellow). Pure yellow in 99.7 per cent alcohol. If 0.1

cc. 0.01 N hydrochloric acid is added to 10 cc. the solution becomes orange-yellow. Upon continued addition of acid the color changes but little toward the red side. Change not sharp (for details *cf.* Kolthoff (27)).

The sensitivity of the alkali-sensitive indicators toward acids may be found in the same way as that of the acid-sensitive indicators toward alkalies.

Alcohol Content, Per Cent	Sensitivity Toward Hydrochloric Acid	
	Methyl Orange	Methyl Yellow
0	0.00002 N	0.00007 N
17	0.00006 N	0.00010 N
28	0.00014 N	0.00022 N not sharp
48	0.00034 N	0.0008 N not sharp
96	0.0024 N	0.006 N not sharp
	Tropeolin 00	Methyl Violet
0	0.0009 N	0.002 N
17	.0013 N	.0027 N
28	.0025 N	
48	.012 N not sharp	.03 N
69	.026 N not sharp	
96	.012 N not sharp	.08 N

Congo Red: This acid in alcoholic solution undergoes slow changes that make it unsuitable as an indicator. For details *cf.* Kolthoff (27).

The change in sensitivity of indicators caused by alcohol was studied in a more quantitative fashion as follows: 25 cc. of conductivity water or 25 cc. of the alcoholic solution was pipetted into small beakers of tall form. The same amount of indicator solution was added to each, and then a known amount of acid or alkali was added to the water until a transition color was produced. Alkali or acid was then added to the alcoholic solution from a Bang's burette until the color was the same in both beakers. All of the experiments were at 11–12°.

The sensitivity ratio (S.R.) of the indicators in water and in alcohol is given in the tabulations. If the ratio is less than 1 the indicator is more sensitive in alcohol toward acid or base; if it is greater than 1 the indicator is less sensitive than in water. It is to be hoped that these experiments may be repeated later with buffer mixtures in alcoholic solution.

ACID-SENSITIVE INDICATORS

Vol. Per Cent of Alcohol	S. R. Sensitivity Ratio for Nitramin	S. R. for Tropeolin 0
10	0.55	1.6
20	0.25	
30	0.13	2.0
40	0.11	3.6
50	0.09	4.8
60	0.08	6.2
70	0.07	8.0
80	0.055	9.0
90	0.055	8.5
95.6	0.06	6.0
99.7	0.06	3.0

The results in the following table are approximate because the experiments were difficult to perform.

Vol. Per Cent	S. R. for Thymol Phthalein	S. R. for Phenol Phthalein	S. R. for Thymol Blue	S. R. for Curcumine
10	1.3	1.15		
20	2.0	.....	2	0.5
30	4	1.5		
39	9	2.7	5	0.3
46.5	18	7.5		
51	24	.....	.....	0.27
59	.....	25	7.5	
68	70	100	.....	0.3
78	125	380	13	
87	200	1000	15	0.4
93.5	200	3000	24	0.4
99	200	3200	24	0.4

ALKALI-SENSITIVE INDICATORS

Vol. Per Cent of Alcohol	S. R. for Methyl Orange	S. R. for Methyl Yellow	S. R. for Tropeolin 00	S. R. for Methyl Violet
10	1.25	1.3	1.15	
19.5	1.55	1.7	1.7	1.75
28.5	2.7	2.8	3.2	4.6
37	4.8	5.0	9	6.8
42	10			
49	16	13.5	25	16
57	28.5	23	47	
65	45	37	69	
72	64	.....	78	
78	.....	70	86	
87	118	96	82	
92	140	98		
99.4	23	20	54	

Vol. Per Cent of Alcohol	S. R. for Bromphenol Blue	S. R. for Thymol Blue (Acid Solution)
10	0.87	1.0
20	0.62	0.95
30	0.45	0.85
40	0.42	0.70
50	0.42	0.64
60	0.17	0.57
70	0.10	0.5
80	0.08	0.4
90	0.02	0.15
95.5	Acid color	0.024
99.7	Acid color	0.011

A brief discussion of the above results is desirable. If the change of S. R. is plotted (*cf.* Figs. 13, 14, 15) we see that:

(*a*) The curves may run a uniform course, i.e., without break. The S. R. may gradually increase or decrease with increasing alcohol concentration, as with phenol phthalein, or may attain a highest or lowest value and then remain unchanged with

increasing alcohol concentration, as, for example, nitramin, thymol phthalein, thymol blue (in acid and alkaline solution), curcumine.

(*b*) There is a maximum or minimum in S. R. at a certain alcohol concentration, as for tropeolin 0, methyl orange, methyl yellow, tropeolin 00. There is an especially strongly marked maximum in case of the azo-indicators. In case of methyl orange the sensitivity toward acids increases so strongly between 95 and 100 per cent that a simple procedure for the determination of the water content of alcohol may be based on this behavior.

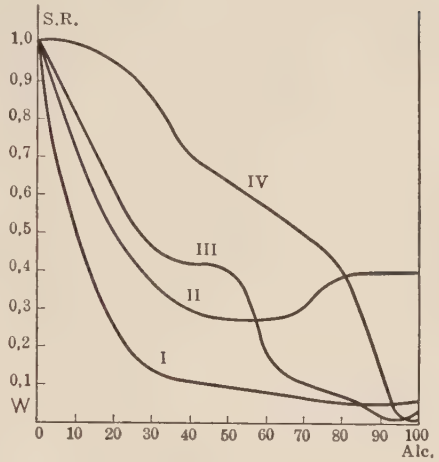


FIG. 13.—I. Nitramine; II. Curcumine; III. Brom phenol blue; IV. Thymol blue (at p_H 3).

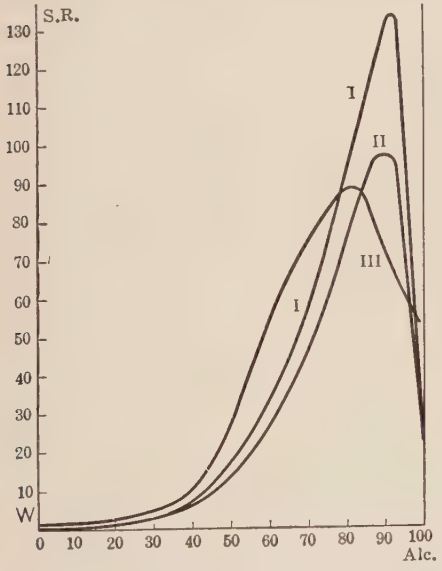


FIG. 14.—I. Methyl orange; II. Methyl yellow; III. Tropeolin 00.

From the detailed experiments and the figures it is evident that tropeolin 0, phenol phthalein, thymol phthalein, thymol blue, and brom phenol blue are more sensitive toward acids in alcohol, whereas nitramine, curcumine, methyl orange, methyl yellow, tropeolin 00, and methyl violet are more sensitive toward alkalies.

From this it may be deduced *that indicators that behave like acids are more sensitive toward hydrogen ion in the*

presence of alcohol regardless of whether the indicator is acid- or alkali-sensitive. Conversely, indicators that are weak bases are less sensitive toward hydrogen-ion in the presence of alcohol. The explanation of this fact lies simply in the fact that alcohol strongly decreases the dissociation constants of the indicators. If we consider an indicator acid, then:

$$\frac{[In^-]}{[HIn]} = \frac{K_{HIn}}{[H^+]}.$$

If we keep $\frac{[In^-]}{[HIn]}$ constant, i.e., maintain the same transition color, then $[H^+]$ must decrease as K_{HIn} decreases; in other words the indicator becomes more sensitive toward hydrogen ion.

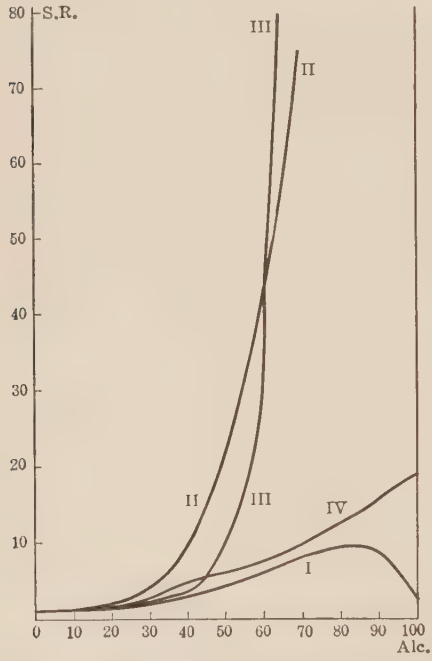


FIG. 15.—I. Tropeolin 0; II. Thymol phthalein; III. Phenol phthalein; IV. Thymol blue.

The quantitative change of sensitivity is controlled both by the repression of the dissociation constants of the indicators and by the decrease in the ionization constant of water. The hydrolysis of the indicator salts is therefore less in alcoholic solution than in water. An indicator acid would thus be less sensitive toward hydrogen ion. But as a matter of fact it is found that indicator acids are more sensitive toward hydrogen ion, from which the conclusion may be drawn that alcohol decreases the dissociation constants of indicators more than it depresses the ionization constant of water. These considerations are of interest in explaining the occurrence of maxima or minima of the S. R. values. The curve for the sensitivity ratio

really consists of the resultant of two others: the one represents the decrease of the dissociation constant of the indicator; the other runs in the opposite direction, and represents the decrease in the ionization constant of water at various alcohol concentrations. Since the relative change in direction of the two curves is not the same at various alcohol contents, it may happen that the relative change in the ionization constant of water at a given alcohol concentration is greater than the decrease in the dissociation constant of the indicator, which is detected by a maximal or minimal value.

It is peculiar that increase of the temperature of alcoholic solutions has just the reverse effect upon the color that is caused by heating an aqueous solution. While an acid indicator like phenol phthalein becomes more acid sensitive in water upon heating, a weak alcoholic solution of the indicator reddens on heating. The reverse is found true upon heating methyl orange, for example. An aqueous solution in the transition range becomes yellow on warming, an alcoholic solution red.

L. Michaelis and M. Mizutani have determined the influence of ethyl alcohol on the dissociation constants of the nitro-indicators. A detailed outline of their results will be given in Chapter V, pages 184 ff.

We will return to the influence of neutral salts and proteins upon the transition interval in an extensive discussion of the colorimetric determination of hydrogen-ion concentration (Chap. V.)

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CHAPTER IV

THE USE OF INDICATORS IN QUANTITATIVE NEUTRALIZATIONS

1. Practically Useful Indicators. Necessary Excess of Reagent.—As is evident from Fig. 9, page 32, in the neutralization of a strong acid with a strong alkali the p_H changes very suddenly near the equivalence-point, going from 3 to 11 during the transition from very feebly acid to weak alkaline reaction. On passing beyond this range by addition of more acid or alkali the p_H changes very slowly. It is therefore probable that indicators whose transition interval lies between p_H 3 and 11 will give a sharp change with strong acids or bases, and that, on the other hand, those indicators whose intervals reach out beyond the stated limits will only show a slow step-by-step change in color. In such cases a considerable excess of acid or base is necessary to pass from neutral solution beyond the limiting color. Such indicators are thus either useless or of use in special titrations only. In the following table the amounts of N, 0.1 N, and 0.01 N acid or base are given that are necessary to give a distinct change from the neutral color of the indicator in 100 cc. of water.

It may be seen from the table that the practically useful indicators for titration of 0.1 N solutions lie *between methyl yellow and thymol phthalein.* We will consider subsequently what indicators are suitable for individual instances and how large the error is in the use of a given indicator.

2. Titration Exponent.—If it is desired to titrate to a given hydrogen ion concentration, the latter is termed the *titration exponent,* p_T, following Bjerrum's (1) usage.

We have seen, in the preceding chapter, to what a large extent the color is dependent upon indicator concentration, especially in case of the one-color indicators. By altering the concentration

NECESSARY EXCESS OF REAGENT IN USING VARIOUS INDICATORS

The excess of acid or alkali that must be present in 100 cc. of aqueous solution to give a perceptible color change is:

	1 N	0.1 N	0.01 N
Thymol blue	0.1 cc.	1 cc.	10 cc.
Tropeolin 00	0.1 cc.	1 cc.	10 cc.
Methyl yellow	0.01 cc.	0.1 cc.	1.0 cc.
Brom phenol blue	0.01 cc.	0.1 cc.	1.0 cc.
Methyl orange	0.008 cc.	0.08 cc.	0.8 cc.
Methyl red	0.000 cc.	0.01 cc.	0.1 cc.
Brom cresol purple	0.000 cc.	0.01 cc.	0.1 cc.
Phenol red	0.000 cc.	0.00 cc.	0.0 cc.
Neutral red	0.000 cc.	0.00 cc.	0.0 cc.
Phenol phthalein	0.002 cc.	0.02 cc.	0.2 cc.
Thymol blue	0.002 cc.	0.02 cc.	0.2 cc.
Thymol phthalein	0.01 cc.	0.1 cc.	1.0 cc.
Alazarine yellow	0.1 cc.	1.0 cc.	10.0 cc.
Nitramin	0.1 cc.	0.8 cc.	8.0 cc.
Tropeolin 0	0.1 cc.	1.1 cc.	11.0 cc.

it is possible to arrive at different titration exponents, using one and the same indicator. Noyes (2) has shown that the color change of a uni-colored indicator is just perceptible when the least perceptible concentration of the colored form $[In_{min.}]$ is one-quarter of the total indicator concentration. The change is therefore visible when 25 per cent of the indicator has changed. We have: $[H^+] = \frac{[HIn]}{[In^-]} \times K_{HIn}$ and hence in the present case for the change:

$$[H^+] = \frac{(4-1)}{1} \times K_{HIn} = 3K_{HIn}.$$

Since the hydrogen exponent belonging to this $[H^+]$ is called the titration exponent p_T we have:

$$p_T = p_{HIn} - \log 3, \text{ or approximately:}$$

$$p_T = p_{HIn} - 0.5.$$

The titration exponent is therefore about 0.5 smaller than the indicator exponent. If, for example, we take 9.7 as the indi-

cator exponent of phenol phthalein, the corresponding titration exponent is 9.2. This holds only for the case when the indicator concentration is so small that a sharp color change is just barely perceptible. If, on the contrary, more phenol phthalein is added, as would be necessary, the color change appears at a smaller p_H value as was shown in the previous chapter. Upon using a solution saturated with phenol phthalein we observe a plain red coloration at about p_H 8.4. It is therefore possible in this case to alter the titration exponent from 9.2 to 8.0 (approx.) by changing the indicator concentration. The change may extend over wider limits when the difference between the solubility and the $[In^-_{mtn.}]$ of the indicator is greater. When the much less soluble substance, thymol phthalein, is used it is possible to titrate to one p_H only, namely a p_T of roughly 9.5.

On the other hand, the transition interval of *p*-nitro phenol may be shifted very appreciably by changing the concentration, as was shown in the previous chapter. Since the region of the titration exponent is rather extended we may titrate to any exponent between 4 and 6.5 by changing the indicator concentration, as Noyes (2) has shown.

The question is more complicated in case of two-color indicators. Noyes has estimated that 5–20 per cent or 80–95 per cent of a two-color indicator must be changed to reach the titration exponent. He found that 5–20 per cent of methyl orange must change from the yellow to the red form before the color is plainly distinct from that of the color of the indicator in pure water. On the other hand 20–30 per cent of the red form must change to the yellow before the color is distinguishable from that of the acid solution. The difference on the two sides of the transition interval is thus explained; the color intensity of the acid form is much greater than that of the basic, and may therefore be detected with greater sensitivity than the basic. In similar manner the author found that a dilute solution of methyl yellow whose yellow color could not be distinguished from that when in pure water was quite plainly rose colored upon acidifying. Only after about fourfold dilution had the rose color become so pale that it was scarcely distinguishable when

placed beside a tube filled with pure water. It may therefore be concluded that the red color is easier to distinguish in the presence of the yellow than vice versa. The color intensity is increased by the chromophoric quinone group in acid solution. About 10 per cent of the methyl yellow must change into the red form before its acid color is perceptible. Then $p_T = 3.0 + \log \frac{90}{10} = 3.95$, or, in other words, the titration exponent of methyl yellow is about 4. The other titration exponent that is found upon starting from the acid side and titrating to alkaline color has less significance because the change is not sharp and the color changes but slowly upon addition of alkali.

In general the influence of concentration on the titration exponent is smaller for two-color than for one-color indicators. Yet it is advantageous not to add too much of a two-color indicator because the color change may be more sharply perceived when the concentration is smaller.

The accuracy with which one may titrate to a given titration exponent is quite high, but depends upon the nature of the indicator. In general, pure indicators should be used rather than naturally occurring products, for the latter might possibly contain other compounds of almost any conceivable kind, that would render the color change indistinct and the transition interval longer. Litmus, for example, consists of a mixture of acids many of which act as indicators. Therefore the transition interval is quite large, extending from about 4.8–8.0. It is not therefore to be recommended as indicator for titrations. It is best to use, for this purpose, indicators with quite short transition intervals so that a sharp color change is observed for small changes in p_H. In general it is possible to titrate with an accuracy of $p_H = p_T \pm 0.2$; this corresponds to a hydrogen-ion concentration of between 1.6 T and $\frac{T}{1.6}$, where T is the hydrogen-ion concentration corresponding to p_T. By using a comparison solution it is possible to titrate to $p_H = p_T \pm 0.1$, corresponding to $[H^+]$ 1.2 T to $\frac{T}{1.2}$.

Upon observing certain precautions it is possible to titrate still more accurately to the correct end-point. These points are discussed extensively in the previously mentioned monograph of Bjerrum.

The best indicator concentrations for titration to a given titration exponent at room temperature are given in the following table:

TITRATION EXPONENTS AND CONCENTRATIONS OF COMMONLY USED INDICATORS

Indicator	p_T	Color	Indicator Concentration
Thymol blue	2.6	Yellowish rose	1 cc. 1% per 100 cc.
Tropeolin 00	2.8	Yellowish orange	1 cc. 1% per 100 cc.
Brom thymol blue	4	Purplish green	0.5– 1 cc. 1% per 100 cc.
Methyl yellow	4	Yellowish orange	0.2–.5 cc. 1% per 100 cc.
Methyl orange	4	Orange	0.2–.5 cc. 1% per 100 cc.
Methyl red	5	Yellowish red	0.2–.5 cc. 2% per 100 cc.
Brom cresol purple	6	Purplish green	0.5– 1 cc. 1% per 100 cc.
Brom thymol blue	6.8	Green	0.5– 1 cc. 1% per 100 cc.
Phenol red	7.5	Rose red	0.5– 1 cc. 1% per 100 cc.
Neutral red	7	Orange red	0.2–.8 cc. 1% per 100 cc.
Cresol red	8	Red	0.5– 1 cc. 1% per 100 cc.
Thymol blue	8.8	Blue violet	0.5– 1 cc. 1% per 100 cc.
Phenol phthalein	8	Pale rose	0.8– 1 cc. 1% per 100 cc.
	9	Pale rose	0.3–.4 cc. 1% per 100 cc.
Thymol phthalein	10	Pale blue	0.5– 1 cc. 1% per 100 cc.
Nitramin	11.6	Orange brown	0.5– 1 cc. 1% per 100 cc.

It should be noted that the use of mixtures of indicators has been proposed in order to make the color change more sharply perceptible. Luther (3) suggested the use of a mixture of methyl orange and indigo carmine instead of methyl orange alone. Moerck (3) has determined the mixture ratio that gives the best results. The following mixture can be recommended: 1 g. of methyl orange and 2.5 g. of indigo carmine were dissolved in 1 l. of water. With this solution the end-point is sharply perceptible even by artificial light. In alkaline solution the color is yellowish green; at the turning point this changes from green through gray to violet. According to the author's experience this mixed indicator is very satisfactory for titrations.

K. C. D. Hickman and R. P. Linstead (4) have proposed the use of a mixture of 1 g. methyl orange and 1.4 g. xylene cyanole red FF in 500 cc. of 50 per cent alcohol. In alkaline solution the color is green, in acid solution magenta red. The solution is steel-gray at the transition point which is reached at a p_H of 3.8.

A. Cohen (3) uses a mixture of the sulphone phthaleins of Clark and Lubs. A mixture of brom cresol purple and brom thymol blue is greenish yellow at $p_H = 6.0$, and pure blue at p_H 6.8. The change is sharp. He also recommends mixtures of brom cresol purple and brom phenol blue, or brom phenol blue and cresol red (*cf.* also Carr (3) and Lizius (3)).

3. Neutralization of Strong Acids with Strong Bases.—If both solution to be titrated and alkali are free from carbonate, it is a matter of indifference what indicator is used with normal solutions, provided the choice is limited to indicators between methyl yellow and thymol phthalein. It may be seen from the table of necessary excesses of reagent that 0.01 cc. of N acid must be added to 100 cc. of neutral solution to produce the perceptible color change of methyl yellow, or 0.01 cc. N alkali to produce a pale blue color in thymol phthalein.

The margin between methyl yellow on one hand and thymol or phenol phthalein on the other thus amounts to 0.02 cc. of normal solution per 100 cc. If 0.1 N solutions are used the necessary excess for methyl yellow is 0.1 cc. 0.1 N acid per 100 cc. and for phenol phthalein 0.02 cc. 0.1 N alkali; the margin is thus 0.12 cc. of 0.1 N. In practice it is found to be greater because sodium hydroxide almost always contains some carbonate. If baryta is used the practically found difference between methyl yellow and phenol phthalein is about 0.10 cc. of 0.1 N solution per 100 cc. The margin is even smaller than 0.12 cc. This is because of the fact that starting with an acid solution the titration with alkali is not carried to the limiting (full alkaline) color of methyl yellow, but to the alkaline color of the aqueous solution.

The necessary excess of acid is smaller than the calculated amount.

The error is greater in the titration of 0.01 N solutions. The amount of 0.01 N acid per 100 cc. of liquid is 1 cc. with methyl

yellow, and with phenol phthalein 0.2 cc. 0.01 N alkali. The margin is thus 1.2 cc. or 1.2 per cent. The difference between methyl red and phenol phthalein is smaller, amounting to 0.3 cc. or 0.3 per cent. It is therefore advisable to use methyl red or phenol phthalein in standardizing 0.01 N acids or alkalies, and to avoid the use of methyl yellow.

In support of this view a table published by Schoorl (5) is given here.

EXPERIMENTS OF SCHOORL

Ratio of Strength of N Acid to N Alkali as 25 : 24.30

After Ten-fold Dilution		Limit of Error, Per Cent
(*a*) Titration to limiting color		
with phenol phthalein	25 : 24.35	0.4
with methyl orange	25 : 24.24	
(*b*) Titration to water (neutral) tint		
with phenol phthalein	25 : 24.30	0.0
with methyl orange	25 : 24.30	

After Hundred-fold Dilution		Limit of Error, Per Cent
(*a*) Titration to limiting color:		
with phenol phthalein	25 : 24.50	3.6
with methyl orange	25 : 23.62	
(*b*) Titration to neutral tint:		
with phenol phthalein	25 : 24.28	0.3
with methyl orange	25 : 24.20	

It is therefore most advantageous to titrate to the color that the indicator gives to neutral water.

The following experiments make clear the error that may result upon using various indicators with 0.01 N solutions. 0.01 N HCl was titrated with approximately 0.01 N baryta water using various indicators. The reverse titration was also studied.

25 cc. 0.01 N HCl required 22.58 cc. of baryta water with methyl yellow.
25 cc. 0.01 N HCl required 22.74 cc. of baryta water with methyl orange.
25 cc. 0.01 N HCl required 22.85 cc. of baryta water with phenol phthalein.

The margin of difference between methyl yellow and phenol phthalein is 0.22 cc. or 0.9 per cent; between methyl red and phenol phthalein 0.07 cc. or 0.3 per cent.

As previously mentioned, a greater difference is found between the values for methyl yellow and phenol phthalein when the solutions are not free from carbonate. Since most sodium hydroxide solutions contain carbonate it is advantageous to establish the titer with different indicators and to use these values when appropriate.

4. Neutralization of Weak Acids with Strong Bases.—It is apparent from Fig. 9, page 32, that in the neutralization of acetic acid with sodium hydroxide the acid is not all used upon titration to the alkaline color of methyl yellow or methyl red. The reaction is not complete until the turning point indicated by phenol phthalein. The behavior of acetic acid is typical of all weak acids. It may therefore be concluded that phenol phthalein must be used in the titration of weak acids with strong bases.

The neutral salt that is formed, sodium acetate in this instance, reacts feebly alkaline or neutral to phenol phthalein, the p_H depending upon the concentration.

N sodium acetate: p_{OH} 4.62, $p_H = 9.57$,

0.1 N sodium acetate: p_{OH} 5.12, $p_H = 9.07$,

0.01 N sodium acetate: p_{OH} 5.62, $p_H = 8.57$.

When the rose color of phenol phthalein is reached we have a solution of the neutral salt. If somewhat more alkali is added the solution changes suddenly to deep red. Now the question arises: How large must the dissociation constant of an acid be in order that it may be accurately titrated using phenol or thymol phthalein? In general this question may be answered by consideration of the hydroxyl-ion concentration, i.e., degree of hydrolysis of the neutral salt formed, and this in turn is dependent upon the concentration. If we use 0.1 N solutions and assume that the p_H of the neutral salt solution may be 9–10, p_{OH}

is roughly 5–4. According to the hydrolysis equation (32) page 15, we have:

$$p_{OH} = 7 - \tfrac{1}{2}\, p_{HA} - \tfrac{1}{2} \log c. \quad . \quad . \quad . \quad . \quad (32)$$

In the present instance a K_{HA} value 10^{-5} or p_{HA} 5 corresponds to $\frac{1}{2} \log c = 0.5$ and $p_{OH} = 5$. At p_{OH} 4, p_{HA} is 7 and $K_{HA} = 10^{-7}$.

The corresponding values derived in like manner for N solutions are:

$$p_{OH} = 5, \qquad K_{HA} = 10^{-4};$$
$$p_{OH} = 4, \qquad K_{HA} = 10^{-6},$$

and for 0.01 N solutions,

$$p_{OH} = 5, \qquad K_{HA} = 10^{-6},$$
$$p_{OH} = 4, \qquad K_{HA} = 10^{-8}.$$

We thus obtain an approximate expression of how large the dissociation constant must be if the acid is subject to titration with phenol phthalein as indicator. Hence hydrocyanic acid may not be titrated using phenol phthalein because its dissociation constant is 10^{-9}. Then in 0.1 N KCN,

$$p_{OH} = 7 - 4.5 + 0.5 = 3; \quad p_H = 11.$$

Phenol and thymol phthalein change long before this p_H. The last calculation does not give an entirely correct picture of the permissible minimum of the dissociation constant because it creates the incorrect impression that this minimum must necessarily be smaller for the titration of a normal solution than for 0.1 or 0.01 N fluids, because the hydroxyl-ion concentration is larger in the normal-salt solution than in the more dilute ones. We have not yet taken the titration error into consideration.

5. Titration Error.—If we titrate 50 cc. of 0.1 N acid with 50 cc. 0.1 N alkali, the total volume being 100 cc. and if p_T 9, i.e., we titrate to $p_H = 9$, and if the permissible error is 0.1 cc. 0.1 N alkali, or 2 per cent, the hydrolyzed solution when the acid is completely neutralized contains both an excess of OH^- and of undissociated acid whose amounts may be calculated from the hydrolysis equation. In a 0.05 N salt solution:

$$p_{OH} = -\log [HA] = 7 - \tfrac{1}{2}\, p_{HA} + 0.65 = 7.65 - \tfrac{1}{2}\, p_{HA},$$

and

$$[HA] = \frac{1.4 \times 10^{-8}}{\sqrt{K_{HA}}}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (96)$$

If an error of 0.2 per cent is permissible this means that at the end of the titration 0.1 cc. of 0.1 N acid per 100 cc. of acid-base mixture still remains to be neutralized. This corresponds to a concentration:

$$[HA] = 10^{-4}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (97)$$

It follows from equations (96) and (97) that the total amount of the undissociated acid is:

$$[HA] = 10^{-4} + \frac{1.4 \times 10^{-8}}{\sqrt{K_{HA}}}. \quad . \quad . \quad . \quad . \quad (98)$$

But the dissociation constant of the acid is:

$$K_{HA} = \frac{[H^+]\,[A^-]}{[HA]}.$$

From which it follows that

$$[HA] = \frac{[H^+]\,[A^-]}{K_{HA}}.$$

Since $[H^+] = 10^{-9}$ and $[A^-] = 5 \times 10^{-2}$ in our instance,

$$[HA] = \frac{5 \times 10^{-11}}{K_{HA}}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (99)$$

Since this value for [HA] must be equal to that calculated from (98), we have:

$$10^{-4} + \frac{1.4 \times 10^{-8}}{\sqrt{K_{HA}}} = \frac{5 \times 10^{-11}}{K_{HA}}, \quad . \quad . \quad . \quad (100)$$

$$K_{HA} + 1.4 \times 10^{-4}\sqrt{K_{HA}} - 5 \times 10^{-7} = 0.$$

Upon solution of this quadratic equation K_{HA} is 4×10^{-7}; $p_{HA} = 6.40$. Hence the dissociation constant may not be smaller than 4×10^{-7} if 0.1 N solutions and a p_T of 9 are specified, and if the titration error may not be greater than 0.2 per cent. If an error of 1 per cent is permissible then naturally K may be smaller. The permissible minimum is then:

$$K_{HA} = \text{about } 10^{-8}; \quad p_{HA} = 8.0.$$

If the calculation is carried out in similar fashion for the minimum value of K_{HA} when $p_T = 10$ and the permissible error is 0.2 per cent, it is found that:

$$K_{HA} = 3 \times 10^{-8} \quad \text{and} \quad p_{HA}\ 7.5.$$

Similar values may be calculated for titration with 0.01 N solutions.

The calculation of the titration error in a given case is simpler when the dissociation constant of the acid is known.

EXAMPLE:—Neutralization of 0.1 N acetic acid with 0.1 N alkali.

(*a*) $p_T = 9$; $p_{HAc} = 4.75$. Calculation shows that the titration is then exactly correct. Working with phenol or thymol phthalein as indicator there is practically no error.

(*b*) $p_T = 7$. Neutralization with neutral red. A calculation shows that we may neglect the amount of HAc present in the neutral salt solution because of repression of hydrolysis. Corresponding to $p_H = 7$, we have:

$$[HAc] = \frac{10^{-7} \times 5 \times 10^{-2}}{10^{-4.75}} = \text{about } 10^{-4}.$$

At an end volume of 100 cc. using 0.1 N solution the error is only 0.1 cc. = 0.2 per cent.

(*c*) $p_T = 6$. This value is obtained in the titration of acetic acid with alkali to the pure yellow color of methyl red.

[HAc] is then about 10^{-3}. The error thus amounts to 2 per cent. Although the transition range of methyl red is traversed gradually, acetic acid may be almost completely neutralized with the indicator by stopping just at the pure alkaline color.

(*d*) $p_T = 4$. Neutralization with methyl yellow. At p_H 4:

$$[HAc] = \frac{10^{-6.5}}{10^{-4.75}} = 2 \times 10^{-2}.$$

Hence with methyl yellow the change is inaccurate and at the wrong region.

In agreement with the calculations it is found that the same values are found in the titration of 0.1 N acetic acid with either neutral red or phenol phthalein.

6. Neutralization of a Weak Base with a Strong Acid.—It may be concluded from Fig. 9, page 32, that phenol phthalein may not be used in the neutralization of weak bases because the change occurs before the alkali is neutralized. An alkali-sensitive indicator such as methyl red or yellow must be used. The titration error may be reckoned in the same way as for acids.

If an end-volume of 100 cc. is considered, with 0.1 N solutions, the dissociation constant of the base may not fall below a certain minimum value, that must be:

for $p_T = 5$, $K_{BOH} =>$ about 4×10^{-7}, $p_{BOH} <$ about 6.4;

for $p_T = 4$, $K_{BOH} =>$ about 3×10^{-8}, $p_{BOH} <$ about 7.5.

If we wish to neutralize a 0.1 N base solution using methyl red, the dissociation constant may not be smaller than 4×10^{-7}; if methyl yellow is to be used, with a maximum permissible error of 0.2 per cent the dissociation constant may not be less than 3×10^{-8}.

This becomes clear upon attempting to neutralize aniline, for example, using methyl yellow or congo red as indicator. Beckurts states that this determination may actually be made. But we have:

$$p_{\text{analine}} = \text{about } 9.5.$$

For $p_T = 3.5$.

$$[BOH] = \frac{[B^+] \times [OH^-]}{K_{BOH}}.$$

Assuming that

$$[B^+] = 5 \times 10^{-2} = 10^{-1.3}, \quad \text{and} \quad [OH^-] = 10^{-10.5},$$

then

$$[BOH] = \frac{10^{-11.8}}{10^{-9.5}} = 10^{-2.3} = 5 \times 10^{-3}.$$

The error that is possible therefore amounts to 10 per cent; furthermore the assumed titration exponent 3.5 is difficult to attain unless a comparison solution is used. It is found, in fact, that titration of aniline with 0.1 N solution and using dimethyl yellow gives useless results. The dissociation constant

of aniline is so small that it can hardly be titrated using indicators. In order to obtain practically useful results tropeolin 00 or thymol blue is used in the titration of normal aniline solution with normal acid (*cf.* page 128).

7. The Neutralization of Polybasic Acids or Polyacid Bases.—When all of the dissociation constants of polybasic acids, or polyacid bases are large, they behave like strong monobasic or acid compounds upon neutralization. Sulphuric acid is a case in point.

The remarks that have been made for strong acids or bases apply equally well to the polybasic or acidic substances in the process of titration to the neutral salt, even when the second dissociation constant is small (e.g., neutralization of oxalic acid to potassium oxalate).

The case is different when the titration is carried to the acid salt stage. For the moment we will omit bases from consideration, for analogous considerations apply to them.

Neutralization to an acid salt may be carried out accurately only when there is a great difference between the two dissociation constants of the acid. It may be deduced in a simple manner that the p_H of such a solution amounts to about half the sum of the two acid exponents. If

$$K_1 = 3 \times 10^{-7}, \quad K_2 = 6 \times 10^{-11} \text{ (carbonic acid)},$$

$$p_1 = 6.5, \qquad p_2 = 10.23.$$

Hence the p_H of a bicarbonate solution is:

$$p_H = \frac{6.5 + 10.23}{2} = 8.37.$$

The p_H of such a solution is actually 8.4 (McCoy (6)). The magnitude of p_T in the titration of carbonic acid as a monobasic acid may be thus simply deduced.

It is much more difficult to derive a generally valid formula for the titration error of polybasic than of monobasic acids. Such derivation will not therefore be attempted here. It is quite simple to deduce the titration error in any given instance of titration to a given p_T value.

If, for example, carbonic acid is to be neutralized as a monobasic acid, we know that the sodium bicarbonate formed dissociates into HCO_3^- and Na^+ in aqueous solution.

The HCO_3^- dissociates further:

$$HCO_3^- \rightleftarrows H^+ + CO_3^=.$$

Hydrolysis occurs at the same time:

$$HCO_3^- + H_2O \rightleftarrows H_2CO_3 + OH^-.$$

A bicarbonate solution contains $CO_3^=$ as well as H_2CO_3.

If acid is added to such a solution it can not be assumed that in the beginning the acid added is equivalent to the H_2CO_3 formed, because $CO_3^=$ ions are neutralized to form HCO_3^- ions.

As has been stated, McCoy found for 0.1 N bicarbonate solution:

$$[H^+] = 4 \times 10^{-9}; \quad \text{hence } p_H = 8.4.$$

Since $[H^+]$ changes only slightly with salt concentration the titration exponent for carbonic acid tiration is in general $p_T = 8.4$. How large will the error be if the titration is carried to $p_H = 8.0$?

The assumption will be steadily that 0.1 N solutions are used, so that the salt concentration is finally 5×10^{-2}.

Now,

$$K_1 = \frac{[H^+] \times [HCO_3^-]}{[H_2CO_3]} = 3 \times 10^{-7}.$$

$$K_2 = \frac{[H^+]\,[CO_3^=]}{[HCO_3^-]} = 6 \times 10^{-11}.$$

Since, in a bicarbonate solution,

$$[H^+] = 4 \times 10^{-9} \quad \text{and} \quad [HCO_3^-] = 5 \times 10^{-2},$$

the author finds for $[H_2CO_3] = 0.6 \times 10^{-3}$.

If the titration is to $p_H = 8.0$, $[H^+]$ is 10^{-8} and therefore

$$[H_2CO_3] = 1.6 \times 10^{-3}.$$

At this $p_T = 8.0$ a certain amount of H_2CO_3 must be neutralized, corresponding to a concentration of $(1.6 - 0.6) \times 10^{-3} = 1 \times 10^{-3}$.

But there is already a certain amount of CO_3-ions present in a bicarbonate solution, whose concentration may be calculated from K_2. If we titrate to the bicarbonate point a certain amount of carbonate has been converted into bicarbonate as well as into carbonic acid. If the titration is carried to a smaller p_H the amount of $CO_3^=$ becomes smaller. The difference between the amount of $CO_3^=$ originally present in the solution and that at the $p_H(= 8)$ found by titration is equal to the alkali addition that is necessary to transform the carbonic acid to bicarbonate.

In 0.05 N bicarbonate solution:

$$[CO_3^=] = \frac{[HCO_3^-]}{[H^+]} \times K_2 = \frac{5 \times 10^{-2} \times 6 \times 10^{-11}}{4 \times 10^{-9}} = 7.5 \times 10^{-4}.$$

At $[H^+] = 10^{-8}$,

$$[CO_3^=] = \frac{3 \times 10^{-12}}{10^{-8}} = 3 \times 10^{-4}.$$

At $p_H = 8.0$ a certain amount of alkali must, as has been shown, be added to transpose a part of HCO_3^- into $CO_3^=$, the amount being equal to a concentration of $(7.5 - 3) \times 10^{-4} = 4.5 \times 10^{-4}$. It was also found that the amount of alkali necessary at $p_H = 8$ to neutralize the $[H_2CO_3]$ present amounted to 1×10^{-3}. The total amount of alkali necessary at $p_H = 8$ corresponds to a concentration of $1 \times 10^{-3} + 4.5 \times 10^{-4} = 1.5 \times 10^{-3}$. This corresponds to an error of 3 per cent in the case at hand. It is evident, therefore, that the titration of carbonic acid as a monobasic acid is not sharp and that it is necessary to add the exact amount of phenol phthalein to bring the $p_T = 8.4$ as accurately as possible. *Cf.* the neutralization curve of carbonic acid, Fig. 16, page 120.

It was known from an earlier investigation (7) that 0.1 cc. of 1 per cent phenol phthalein solution had to be used per 100 cc. to obtain good results in the titration of free carbonic acid. From the table of titration exponents of various indicators it is evident that this amount actually corresponds to a p_T of 8.4-8.5. If a different amount of phenol phthalein is used and titration is carried to the first rose color, a correction must be applied.

In this kind of titration the amount of indicator is of considerable significance. What has been said in case of carbonic acid holds also for phosphoric acid. The exponent for titration as a dibasic acid is $p_T = 9.3$. Good results are only obtained with the right ratio of phenol phthalein; it is better to use thymol phthalein (8).

If phosphoric acid is titrated as a monobasic acid the equivalence-point (see Fig. 16) is reached at $p_T = 4.2$. Methyl yellow shows an alkaline transition color at this hydrogen-ion concen-

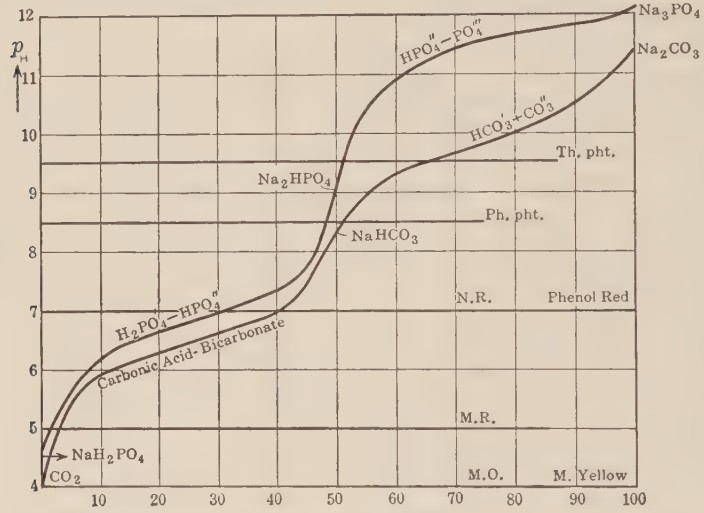

FIG. 16.

tration, so that it is best to work with a comparison solution of primary sodium phosphate containing the same amount of indicator; either brom phenol blue or methyl orange—indigo carmine mixture may also be used. The error that results upon titration to a different p_H may be calculated in the same way as was done for carbonic acid. The error caused by undissociated phosphoric acid must be considered, and also that due to the secondary sodium phosphate:

$$H_2PO_4^- + H_2O \rightleftarrows H_3PO_4 + OH^-,$$

$$H_2PO_4^- \rightleftarrows H^+ + HPO_4^{=}.$$

The reader is referred to the original literature (9) concerning the acidimetric determination of sulphurous and pyrophosphoric acids.

It should be noted, finally, that titration exponent and the titration error may be calculated from the dissociation constants as has been shown above; it is more convenient, however, to determine these quantities experimentally.

8. Titration of a Mixture of a Medium Strong and a Weak Acid, or of Analogous Mixtures of Bases.—The magnitude of the hydrogen exponent at the first equivalence-point in the titration of a mixture of a medium strong and weak acid with alkali has been calculated in Chapter I, 9, d. It was found that at this point

$$p_H = p_T = \tfrac{1}{2}(p_{K_1} + p_{K_2}), \quad . \quad . \quad . \quad . \quad . \quad (64)$$

if both acids have the same concentration.

Although the titration exponent may be conveniently calculated from this equation, it yields no information about the accuracy of the titration. The smaller the buffer capacity, or in other words, the greater the change in p_H upon addition of a small amount of base the more exact will be the result.

As will now be shown, in harmony with our expectations, the accuracy of the titration depends upon the ratio of the dissociation constants of the two acids. The larger this ratio the sharper the color change of an appropriate indicator. To illustrate, it is again assumed that both acids have the same concentration, and it will be shown to what extent the hydrogen-ion concentration at the first equivalence-point is changed by addition of 1 per cent excess of alkali (i.e., 1 per cent of the concentration of one of the acids) or 1 per cent of the medium strong acid, at various ratios of the two constants K_1 and K_2. The following derivations continue those that were given on page 35.

If the ratio of the two dissociation constants is known the following relation may be written at once from equation (62):

$$\frac{[H_1A_1]}{[A_1^-]} : \frac{[H_2A_2]}{[A_2^-]} = \frac{K_2}{K_1} \quad . \quad . \quad . \quad . \quad . \quad (62)$$

If the sum of $[H_1A_1] + [A_1^-]$ is set equal to 100, then we may find in like manner how large the values of a and $(100 - a)$ are in equation (63).

As has been mentioned, the acid H_1A_1 is not completely transformed into its salt at the first equivalence-point; an amount $(100 - a)$ per cent is still present as free acid. The second acid H_2A_2 is transformed into its salt to this extent. If an excess of alkali of 1 per cent is now added at the first equivalence-point a further portion of the acid H_1A_1 is neutralized and the remainder of the alkali is bound by H_2A_2. If the part which is used for the neutralization of H_1A_1 is x per cent of the amount of H_1A_1 that was originally present, then:

$$[A^-] = a + x,$$

and

$$[H_1A_1] = 100 - (a + x),$$

while

$$[A_2^-] = 100 - (a + x) + 1,$$

and

$$[H_2A_2] = a - x.$$

If we substitute these values in equation (63), then we find that:

$$\frac{100 - (a + x)}{a + x} \times \frac{101 - (a - x)}{a - x} = K_2 : K_1 \quad . \quad (101)$$

If $K_2 : K_1$ is known, x may be calculated from the quadratic equation. Hence $[A^-]$ and $[H_1A_1]$ may be deduced and $[A^-]$ is found as follows:

$$[H^+] = \frac{[H_1A_1]}{[A_1^-]} \times K_1.$$

EXAMPLE: $K_1 : K_2 = 100$.

At the first equivalence-point $a = 91$, and thus

$$[H^+] = \frac{9}{91} K_1 = 0.099\ K_1.$$

Upon the addition of 1 per cent of alkali $[A^-]$ becomes $91 + x$ $[H_1A_1] = 9 - x$. $[A_2^-] = 10 - x$, and $[H_2A_2] = 91 - x$.

Upon substituting this value in (101) we find.

$$x = 0.4.$$

Hence upon addition of 1 per cent alkali $[H^+]$ has become:

$$[H^+] = \frac{8.6}{91.4} K_1 = 0.094\, K_1.$$

At the first equivalence-point $[H^+]$ was $0.99K_1$ and therefore addition of 1 per cent excess of alkali has made its value only 5 per cent smaller. This change corresponds to an increase in p_H of about 0.02. Since this small change can not be detected very well colorimetrically, it follows that the titration will not give good results if the ratio is equal to 100. When the ratio is 10^4, p_H at the first equivalence-point changes from

$$10^{-2}K_1 \text{ to } 6.2 \times 10^{-3}K_1.$$

$[H^+]$ therefore becomes 38 per cent smaller, corresponding to a change of 0.21 in p_H.

A change of this magnitude may be determined readily using a reference solution; *it may be concluded therefore that the titration of* H_1A_1 *in presence of an equal concentration of* H_2A_2 *is possible to an accuracy of* 1 *per cent if the ratio of* $K_1 : K_2$ *is equal to or greater than* 10^4. *The greater this ratio, the sharper the change.*

If, for example, $K_1 : K_2 = 10^6$, the hydrogen-ion concentration at the first equivalence-point is changed from $10^{-3}K_1$ to $10^{-4}K_1$, which corresponds to a change of 1 in p_H. In this instance the titration may be made with an accuracy of 0.2 per cent. If the acids H_1A_1 and H_2A_2 have different initial concentrations the above limits are changed.

It should be noted that almost the same considerations that apply to mixtures of acids of different dissociation constants also apply to the titration of polybasic acids.

The same considerations that have been given for acid mixtures naturally apply to mixtures of bases with widely different dissociation constants. Instead of p_H we find p_{OH} in the calculations, and hence p_H may be directly deduced:

$$p_H = p_{H_2O} - p_{OH}.$$

These considerations are illustrated by the following results of individual titrations.

Mixture of 0.1 N acetic and 0.1 N boric acids.

$$K_1 = 1.8 \times 10^{-5}, \quad K_2 = 6 \times 10^{-10}, \quad K_1 : K_2 = 3 \times 10^{-4}.$$

From these values p_H calculated for the first equivalence-point is 6.99, while the value found in other ways is 6.95. Titration of a mixture of 25 cc. 0.1 N acetic acid and 25 cc. 0.1 N boric acid using neutral or phenol red. $p_T = 7.0$. 25 cc. 0.1 N alkali are bound. The titration may easily be carried out with an accuracy of 0.4 per cent.

Mixture of 0.1 N tartaric and 0.1 N boric acids. $K_1 : K_2 = 1.2 \times 10^5$, titration readily made with 0.2 per cent accuracy, $p_T = 6.5$ with cresol purple as indicator.

Mixture of 0.1 N citric with 0.1 N boric acid. $K_1 : K_2 = 3.2 \times 10^3$. Titration reliable to about 1 per cent. $p_T = 7.5$ with phenol or neutral red as indicator.

Mixture of 0.1 N primary phosphate and 0.1 N boric acid. The titration is not possible because the ratio of the second dissociation constant of phosphoric acid to that of boric acid is 3.3×10^2. The color of phenol phthalein is already very pale rose at the first equivalence-point. Upon addition of more alkali the color increases very slowly in intensity. If the titration is carried to the first perceptible color change of phenol phthalein the accuracy of the titration does not exceed 2–3 per cent.

Mixtures of weak bases with very different dissociation constants may also be titrated in this way. The titration of ammonia in presence of pyridine, for example, has practical significance.

$$K_1 : K_2 = 1.2 \times 10^4, \quad p_T = 7.4;$$

Indicator: neutral red or phenol red.

Accuracy about 0.5–1 per cent. If the two bases are to be titrated together, methyl yellow, methyl orange, or brom phenol blue, is used, and $p_T = 3.5$. For details see Tizard and Boeree (10) and Kolthoff (10).

From the foregoing discussion it is clear that it may be predicted in advance whether a mixture of acids or bases with divergent dissociation constants may be titrated accurately in the presence of each other, or simultaneously, and that the

magnitude of the titration exponent may be deduced from the dissociation constants.

9. The Neutralization of Weak Acids with Weak Bases.—As may be seen from Fig. 10 (page 35) the neutralization curve of acetic acid with ammonia shows in general a nearly level course. Only between p_H 6.5 and 7.5 in the region of the equivalence-point is it nearly vertical. It is therefore to be expected that the neutralization of acetic acid with ammonia, or the reverse, can not be made with either acid- or alkali-sensitive indicators. If the titration is made to the alkaline color of methyl red there is still 3 per cent of free acetic acid present, whereas with phenol phthalein there is always an appreciable amount of free ammonia in solution. In this case only neutral red or another similar indicator may be used. The titration exponent for acetic acid—ammonia is 7.0. It is therefore best to use a reference solution of $p_H = 7.0$. The change is not very sharp, but with practice a considerable degree of accuracy may be attained (*cf.* the next table).

In similar fashion other weak acids may be titrated with ammonia or other weak bases (11). The titration exponent is based on the hydrogen exponent of the neutral salt. It is assumed here that the dissociation constants of acid and base are not appreciably smaller than 10^{-6}, since the influence of hydrolysis would then increase the error to too large an extent. The titration error may be calculated in the same way that was used for carbonic acid. Some results of experiment are given here.

Titration of 25 cc. of 0.1 N acetic acid with 0.1 N ammonia.

Indicator	Found	Deviation, Per Cent
Neutral red	24.96	−0.16
$p_T = 7.1$	25.00	0.0
Phenol phthalein	25.85	+3.4
$p_T = 8.0$	25.80	+3.2
Methyl red	24.30	−2.8
$p_T = 6.2$	24.25	−3.0

The titration with neutral red goes very well if a comparison solution of the same p_H as the titration exponent is used. Phenol phthalein and methyl red are useless in this case.

10. Titration of Bound Alkali in a Salt of a Weak Acid, and of Bound Acid in the Salt of a Weak Base.—As is well known, the alkali in the salt of a weak acid may be determined by titration with hydrochloric acid, provided the acid of the salt is so weak that it does not impart an acid transition color to the alkali-sensitive indicator used. Methyl yellow, for example, imparts a pale acid transition color to a saturated solution of carbonic acid, and is therefore unsuitable for the titration of alkali combined with carbonic acid. We will now find how large the dissociation constant of the acid may be if the titration in 0.1 N solution is to be sharp with error not exceeding 0.2 per cent.

If the hydrogen-ion concentration of the acid solution is not greater than 10^{-4} we may calculate roughly the maximum value of the dissociation constant for sufficiently accurate titration. If the total concentration of undissociated acid at the end of the titration is again 5×10^{-2}, i.e., 0.1 N solutions are used, then it follows from the equation:

$$\frac{[H^+]\,[A^-]}{[HA]} = K_{HA},$$

how large K_{HA} maximum may be.

Since $[H^+] = [A^-] = 10^{-4}$, and $[HA] = 5 \times 10^{-2}$, K_{HA} is $= < 2 \times 10^{-7}$, $p_{HA} = > 6.30$.

If the hydrogen-ion concentration at the end of the titration may not exceed 10^{-5}, then:

$$K_{HA} = < 2 \times 10^{-9}, \quad p_{HA} = > 8.30.$$

The titration error may be calculated simply from K_{HA}. The basic assumption is that the error may be at most 2 per cent, and hence at most 2 per cent of undecomposed salt may be present. If $p_T = 4.0$, it is found that:

$$[A^-] = \frac{5 \times 10^{-2}}{10^{-4}} \times K_{HA}.$$

This $[A^-]$ does not agree exactly with the concentration of the still undecomposed salt because the solution of the weak acid also contains some anions at the end-point. The latter amount must be subtracted from the above value; it may be calculated simply; in the acid solution:

$$[H^+]^2 = [A^-]^2 = \sqrt{K_{HA} \times HA},$$

$$[A^-] = 2.2 \times 10^{-1}\sqrt{K_{HA}}.$$

At a p_T of 4 the concentration of $[A^-]$, yielded by the undecomposed salt is:

$$[A^-] = \frac{5 \times 10^{-2}}{10^{-4}} \times K_{HA} - 2.2 \times 10^{-1}\sqrt{K_{HA}} . \quad (102)$$

Since an error of 2 per cent was stipulated, $[A^-]$ in the titration of 0.1 N solution is 10^{-4}. From this value and equation (102) it follows that:

$$5 \times 10^{-2} K_{HA} - 0.22\sqrt{K_{HA}} = 10^{-4}.$$

Hence

$$K_{HA} = < 5 \times 10^{-7}, \quad p_{HA} = > 6.3.$$

It may be calculated in the same way how large K_{HA} may be at $p_T = 5$ and a limiting error of 2 per cent. It is thus found that:

$$K_{HA} = 2.5 \times 10^{-8}, \quad \text{and} \quad p_{HA} = 7.6.$$

If combined alkali is to be titrated in 0.1 N solution using methyl yellow ($p_T = 4$), then:

$$K_{HA} \text{ must be } = > 5 \times 10^{-7} \quad \text{and} \quad p_{HA} = <6.3;$$

if methyl red is used ($p_T = 5$),

$$K_{HA} \text{ must be } = < 2.5 \times 10^{-8}, \quad p_{HA} = > 7.60,$$

with an upper limit of error of 2 per cent.

The maximum value of the dissociation constant for other concentrations may be calculated similarly. If the particular salt is insoluble, the concentration of the undissociated acid soon reaches a maximum and remains constant. It should be considered in the calculation that [HA] agrees with the concentration of the saturated solution. Thus the maximum value of con-

centration of carbonic acid in water at room temperature is 5×10^{-2} molar.

Conversely, it is very simple to find by calculation how large the dissociation constant of a base may be if the combined acid of its salt is to be titrated with alkali using thymol phthalein or phenol phthalein. Again assuming an error of 2 per cent for 0.1 N solution, and $p_T = 9.0$, we obtain:

$$K_{BOH} = < 2.5 \times 10^{-8}, \quad p_{BOH} = > 7.6,$$

and at $p_T = 10$:

$$K_{BOH} = < 5 \times 10^{-7}, \quad p_{BOH} = > 6.3.$$

These deductions are capable of manifold application. It may be concluded, for example, that alkali bound as carbonate or bicarbonate may not be determined using methyl red because the error would be too great. Methyl yellow, however, is excellent for this purpose. A. Richter (12) determined the influence of carbonic acid on methyl yellow in the presence of salts. These data are not, however, of great practical importance because the carbonic acid content of an acidified carbonate solution changes rapidly when the solution is exposed to the atmosphere. On the other hand, the alkali bound to boric or hydrocyanic acid may be determined excellently, using methyl red, if we choose a p_T that agrees with the p_H of the aqueous solution of the acid that is present at the end of the titration.

The titration of acid combined with weak alkali may also be determined. Thus salts of aluminum and some other metals may often be titrated easily with phenol phthalein under controlled conditions. Acids combined with aniline, the alkaloids, etc., may be determined by titration by observing the titration exponent. The titration error may be calculated from the known p_T in any given instance.

11. Titration of N Acids or Bases.—Thus far solutions as dilute as 0.1 N have been continually assumed. It may be simply shown that many titrations may be carried out with N solutions that are not sufficiently exact with 0.1 N solutions (13). On page 113 we have seen that the titration of a base with methyl

yellow as indicator and 0.1 N solution of acid may be made with an accuracy of 2 per cent if the dissociation constant is greater than 3×10^{-8}. If it is smaller the titration error becomes greater. If we assume that a less acid sensitive indicator is used in this case the change with 0.1 N acid is very difficult to distinguish in the region of the equivalence-point (*cf.* page 106). If, on the other hand, a 1 N solution of a weak base of dissociation constant 10^{-9} is titrated with N hydrochloric acid, the determination may be very easily made with an accuracy of 2 per cent if acid is added until the first deviation from the color of the indicator in water is noted. In the same manner that was used in calculation of the titration error it may be deduced that bases of dissociation constant down to 10^{-10} are still capable of titration to 1 per cent accuracy using tropeolin 00. A reference solution of p_H identical with that of the solution at the equivalence-point must be used. If the dissociation constant of the base is known, the p_H may be calculated simply from the hydrolysis equation.

It may likewise be deduced that base combined with an acid may be titrated with 1 per cent accuracy using tropeolin 00 if the dissociation constant of the acid is smaller than 10^{-4}, naturally on condition that suitable reference solutions are used and that the reagents are normal. Upon titration of 1 N alkali acetate with N acid the author found 25.05, 25,04, and 25.10 cc. acid, respectively. Either 0.5 N acetic acid or 0.003 N hydrochloric may be used as reference liquid in this case. Alkali combined with formic acid may be determined with an accuracy of 1–2 per cent. It is of practical importance that bases such as aniline, urotropin, etc., may easily be determined with an accuracy of 0.5 per cent. All that has been said about the use of normal acid holds, mutatis mutandis, for the use of normal bases. With tropeolin 0 or nitramin as indicator and using suitable reference solutions, weak acids whose dissociation constants are not smaller than 10^{-10} may be determined with an accuracy of 1 per cent; also acids that are bound to bases of dissociation constant smaller than 10^{-4}. It should be noted that the reference solutions should not be prepared by diluting

sodium hydroxide because traces of carbon dioxide from the air may have a very great effect on the color. Hence solutions of sodium carbonate are more useful.

Titration with N NaOH is practically important in the determination of boric acid and phenols. It is quite significant for the investigation of fertilizers that acids combined with ammonia may be determined with N reagents using tropeolin 0, or better nitramin as indicator.

The maximum limit of error, i.e., 1 per cent, is found in cases in which the dissociation constants reach the limiting values given above. If the conditions are more favorable the errors are smaller (*cf.* Kolthoff (10)).

Although it may easily be seen from the table at the end of this book, and the typical cases developed in this chapter, what acids and bases may be determined under given conditions with permissible accuracy, the following tables are given to simplify the use of these ideas. In the construction of the tables it was assumed that acids are always to be titrated with strong bases, and bases with strong acids. It is not possible to give the exact titration exponent because this is only valid for a given concentration of acid or base.

Acids that are bound to heavy metals or alkaloids are in general titrated with phenol phthalein as indicator. In titrating alkaloid salts with alkali the addition of alcohol or chloroform is usually necessary.

Acids bound to ammonia may be determined in N solution with N alkali using nitramin as indicator.

The dibasic acids that have been mentioned are not in general able to be titrated as monobasic acids using indicators. The following acids behave differently toward different indicators with respect to their titration acidity.

Phosphoric and arsenic acids:

As monobasic acids to M. Y., M. O. or B. P. B. with primary phosphate as comparison solution. As dibasic acids to Th. pht. Ph. pht., and Th. B. are able to be used when the solution is saturated with table salt. May be titrated as a

tribasic acid using Ph. pht. or Th. B. with much calcium chloride present.

ACIDS THAT MAY BE DETERMINED BY TITRATION

Acids	Indicator
Strong acids	Any indicator
Formic, and homologues	Ph. Pht.; Th. B.; Ph. R.; N. R.
Oxalic, and homologues	Ph. Pht.; Th. B.; Ph. R.; N. R.
Hydrofluoric	Ph. Pht.; Th. B.; Ph. R.; N. R.
Boric, with polyvalent alcohols	Ph. Pht.; Th. B.;
Boric, without polyvalent alcohols	Nitramin; Tr. 0. cf. page 128.
Chromic	Ph. Pht.; Th. B.
Hydrocyanic	Nitramin; Tr. 0.
Aliphatic oxy-acids	Ph. Pht.; Th. B.; Ph. R.; N. R.
Tri-chlor-acetic	Any indicator
Benzoic and homologues	Ph. Pht.; Th. B.
Salicylic	Ph. Pht.; Th. B.; Ph. R.; N. R.
Cinnamic	Ph. Pht.; Th. B.
Picric	Ph. Pht.; Th. B.; Ph. R.; N. R.
Gallic	M. R. (not Ph. Pht.; Th. B.)
Hippuric	Ph. Pht.; Th. B.
Phthalic	Ph. Pht.; Th. B.
Uric	Ph. Pht.; Th. B.
Saccharin	Ph. Pht.; Th. B.; Ph. R.; N. R.; M. R.

Ph. pht. = phenol phthalein; Th. B. = thymol blue; Ph. R. = phenol red; N. R. = neutral red; M. R. = methyl red; Tr. 0. = Tropeolin 0.

Phyrophosphoric acid:

As dibasic acid using M. Y., M. O., or B. P. B. to $p_T = 4.0$. As tetra-basic acid with Ph. pht., Th. pht., or Th. B. in presence of enough barium salt.

Carbonic acid:

As monobasic acid using Ph. pht. or Th. B. in presence of enough table salt or glycerine. As dibasic acid in presence of enough barium salt using Ph. pht. or Th. B.

Sulphurous acid:

As monobasic acid with M. Y., M. O., or B. P. B. Dibasic acid in presence of enough barium salt with Ph. pht. or T.B.

Glycerophosphoric acid:

As monobasic acid with M. Y., M. O., or B. P. B. As dibasic acid with Ph. pht. or Th. B.

BASES THAT MAY BE DETERMINED BY TITRATION

Nature of Base	Indicator
Base Bound to:	
Boric acid	M. O.; M. Y.; B. P. B.; M. R.; B. C. P.
Carbonic acid	M. O.; M. Y.; B. P. B.
Hydrogen sulphide	M. O.; M. Y.; B. P. B.; M. R.; B. C. P.
Phosphoric acid to prim salt	M. O.; M. Y.; B. P. B.
Acetic acid, etc.	Tr. 00 with 1 N HCl and acetic acid as a reference liquid (*cf.*, p. 128)
Free Bases:	
Strong bases	All indicators
Ammonia	M. R.; B. C. P.; M. O.; M. Y.; B. P. B.
Aniline	Tr. 00 (*cf.*, p. 112)
Hydrazine	M. R.; M. O.; M. Y.; B. C. P.; B. P. B.
Amines	M. R.; B. C. P.; M. O.; M. Y.; B. P. B.
Aconitine	M. R.; M. O.; M. Y.; B. P. B.
Brucine (monacid)	M. R.; B. P. B. (with 50% alcohol)
Cinchona alkaloids (monac.)	M. R.; B. C. P.
Quinoline	Tr. 00.
Cocaine	M. R.; B. C. P.; M. O.; M. Y.; B. P. B.
Emetine	M. R.; B. C. P.; M. O.; M. Y.; B. P. B.
Hexamethylene tetra-ammine	Tr. 00 (*cf.*, p. 128)
Coniine	M. R.; B. C. P.; B. T. B.; M. O.; M. Y.; B. P. B.
Narcotine	M. O.; M. Y.; B. P. B.
Papaverine	M. R.; M. O.; M. Y.; B. P. B.
Morphine	M. R.; M. O.; M. Y.; B. P. B.
Piperazine	M. O.; M. Y.; B. P. B.
Atropine	M. R.; M. O.; M. Y.; B. P. B.
Pilocarpine	M. R.; B. C. P.
Sparteine	M. R.; B. C. P.; B. T. B.; M. O.; M. Y.; B. P. B.
Strychnine (monacid)	M. R.; B. C. P.; B. P. B. (with alcohol)

Th. pht. = Thymol phthalein; Ph. pht. = phenol phthalein; Th. B. = thymol blue; B. T. B. = brom thymol blue; B. C. P. = brom cresol purple; M. R. = methyl red; M. Y. = methyl yellow; B. P. B. = brom phenol blue; Tr. 00 = Tropeolin 00.

For a full discussion of the titration of alkaloids and their salts see Kolthoff (14).

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CHAPTER V

THE COLORIMETRIC DETERMINATION OF HYDROGEN-ION CONCENTRATION

1. The Basis of the Procedure lies in the fact that every indicator has a transition interval within which its color changes with change in hydrogen-ion concentration. If the p_H of a given solution is to be determined a suitable indicator is added, i.e., one that assumes a transition shade; then the hydrogen exponent is derived by comparison of this color shade with that of the indicator in solutions of known p_H. It is therefore a comparison procedure whose accuracy depends primarily upon the correctness of the reference solutions (standards). The p_H of the latter is determined with the hydrogen electrode. The standardization with the hydrogen electrode is therefore the primary procedure, upon which the whole colorimetric procedure rests. It will be shown subsequently that presence of foreign substances may cause deviations from the correct value when the colorimetric procedure is used.

2. Standard Solutions.—The hydrogen exponent of the reference solutions must be determined with the highest accuracy. The procedure of Michaelis (1) is not to be recommended. He calculates the p_H-value of various buffer mixtures, e.g., acetic acid—sodium acetate or ammonia—ammonium chloride, with the aid of the dissociation constants of the acids and bases. S. P. L. Sörensen (2) performed a specially useful and fundamental service in establishing a series of buffer mixtures with widely ranged p_H-values. He determined the hydrogen exponent of these solutions with the hydrogen electrode. Walpole (3) later measured the p_H-values of sodium acetate—acetic acid mixtures; Palitzsch (4) studied the system boric acid—borax; Clark and Lubs (5)

have established a scale of buffer mixtures whose p_H rises in increments of 0.2 unit from 2.0 to 10.0.

As has been shown in the first chapter, the buffering value of mixtures of a weak acid or base with its salt is not equally effective in all cases. The equalizing action is strongest in a solution where $p_H = p_{HA}$, i.e., one that contains equivalent amounts of acid and salt (see the views of Donald D. Van Slyke, page 24). In this case the hydrogen exponent only changes slightly with small irregularities in composition. The greaters the difference between p_H and p_{HA}, the smaller is the buffering power, and finally at $p_H = p_{HA} \pm 2$ the solution has almost lost buffering power. This fact must be taken into account in using various buffer mixtures.

It is recommended that a mixture of acids of slightly different dissociation constants be used in the preparation of buffer mixtures of great buffer capacity at various compositions (page 29).

The Clark and Lubs (5) mixtures are very simple to prepare. The original materials may easily be obtained in pure form, and the equal differences in p_H-value,—about 0.2 unit,—offer practical advantages.

The chemicals that are necessary for the buffer mixtures of Clark and Lubs (5) may in general be obtained simply in pure form (*vide infra*).

The situation is less favorable with the various primary substances that Sörensen (2) used. The substances may be obtained in pure form from Kahlbaum, but there is no check as to purity. It is not possible to rely on the secondary sodium phosphate of Kahlbaum to contain exactly two molecules of water of crystallization. A determination of the residue on heating is necessary as a check.

Nevertheless the mixtures recommended by Sörensen are accepted here because the hydrogen exponents of the solutions that he recommended have been determined with high accuracy. Furthermore Walbum (6) has determined the change in p_H between 10° and 70° for various members of this series, so that we now have data for the p_H of the standard solutions at temperatures other than 18° and 25°. The change in p_H with changing

temperature runs very regularly so that the value of p_H at any temperature between 10° and 70° may be found by a straight line interpolation. The author has given in the table the values at 40° for the sake of convenience. A table of Palitzsch (7), that has very exactly determined values of p_H for mixtures of boric acid (mixed with some potassium chloride) and borax, is also reproduced. Further, since mixtures of soda and hydrochloric acid are easy to prepare and have good buffering action and are stable, the p_H-values of a series of these systems are given. These were determined by means of the hydrogen electrode by the author in collaboration with Prof. W. E. Ringer (8) in the Utrecht physiological laboratory. Finally a series of p_H-values of mixtures of secondary phosphate with sodium hydroxide, are drawn from the work of Ringer (8), so that buffer mixtures of value p_H 11–12 are also included. In the following pages standard solutions are also considered. Those of Clark and Lubs are especially recommended.

Purity of the Preparations. Hydrochloric acid and sodium hydroxide, carbonate-free, are prepared according to the usual volumetric procedures. *Potassium biphthalate* is obtained according to Dodge (7) with small deviations from the procedure of Clark and Lubs (5), by dissolving 60 g. potassium hydroxide (containing little carbonate) in 400 cc. of water and adding 50 g. of orthophthalic acid or twice as much twice-sublimed phthalic anhydride. The solution is then brought to weak alkaline reaction toward phenol phthalein using phthalic acid or potassium hydroxide, and then an equal amount of phthalic acid is added. Care should be taken that the amount added is equal since otherwise the biphthalate will contain excess of either phthalate or acid. The boiled solution is filtered hot and the potassium biphthalate is obtained by crystallization upon cooling the solution with thorough shaking. The filtered salt is recrystallized at least twice and dried at 110–115°. According to Dodge the crystallization may not be made below 20° because an acid salt is then formed.

BUFFER MIXTURES

Primary Solutions	Investigators	From p_H
I. 0.1 N hydrochloric acid with 0.1 N KCl (7.46 g. per l.)	Clark and Lubs (5)	1.0 – 2.2
II. 0.1 N HCl with 0.1 N K-biphthalate (20.42 g. per l.)	Clark and Lubs (5)	2.2 – 3.8
III. 0.1 N sod. hydroxide with 0.1 N K-biphthalate	Clark and Lubs (5)	4.0 – 6.2
IV. 0.1 N sod. hydroxide with 0.1 N K biphosphate (13.62 g. per l.)	Clark and Lubs (5)	6.2 – 8.0
V. 0.1 N sod. hydroxide with 0.1 N boric acid (6.20 g. per l.), 0.1 N KCl (7.46 g. per l.)	Clark and Lubs (5)	8.0 –10.0
VI. 0.1 N HCl with 0.1 N glycocoll (7.505 g. per l.) and 0.1 N NaCl (5.85 g. per l.)	Sörensen (2)	1.04– 4.0
VII. 0.1 N NaOH with 0.1 N glycocoll (7.505 g. per l.) and 0.1 N NaCl (5.85 g. per l.)	Sörensen (2)	8.24–10.48
VIII. 0.15 N K biphosphate (9.078 g. per l.) and 1.15 N $Na_2HPO_42H_2O$ (11.88 g. per l.)	Sörensen (2)	6.0 – 8.0
IX. 0.1 N sec. Na-citrate (from citric acid) with 0.1 N HCl	Sörensen (2)	2.97– 4.96
X. 0.1 N sec. sod. citrate with 0.1 N NaOH	Sörensen (2)	4.96– 6.3
XI. 0.1 N borax (19.10 g. per l.) with 0.1 HCl	Sörensen (2)	8.0 – 9.24
XII. 0.1 N Borax with 0.1 N NaOH	Sörensen (2)	9.24–10.0
XIII. 0.1 N borax with 0.2 N boric acid and 0.05 N NaCl (12.40 g. boric acid and 2.925 g. NaCl per l.)	Palitzsch (7)	7.60– 9.24
XIV. 0.1 N HCl and 0.2 N Na_2CO_3 (10.60 g. per l.)	Kolthoff	10.0 –11.2
XV. 0.15 N sec. sod. phosphate and 0.1 N sod. hydroxide	Ringer (8)	11.0 –12.0
XVI. 0.05 molar succinic acid and 0.05 molar borax	Kolthoff (1925)	3.0 – 5.8
XVII. 0.1 molar primary phosphate and 0.05 molar borax	Kolthoff (1925)	5.8 – 9.2

Primary Sodium or Potassium Phosphate: Sörensen used a Kahlbaum preparation of potassium phosphate. It was found that primary sodium phosphate may be used without changing the p_H. The commercial preparation is simply crystallized two

or three times from water and dried at 110° to constant weight. When dried at 100° and 20–30 mm. pressure it should not lose more than 0.1 per cent; loss on ignition 13.23 ± 0.1 per cent.

Secondary Sodium Phosphate: Sörensen used a Kahlbaum preparation of $Na_2HPO_42H_2O$ without further test. The author starts with a commercial preparation with twelve molecules of water that is thrice fractionally crystallized and then dried to constant weight over calcium chloride in an exsiccator. It then has the desired composition, $Na_2HPO_42H_2O$. When dried at 100° and 20–30 mm. pressure the loss in weight of the salt is 25.28 ± 0.1 per cent. See N. Schoorl (10) on the preparation of the di-hydrate.

Boric Acid: The commercial preparation is recrystallized at least three times from water and then dried in thin layers between filter paper, and finally a short time in the oven at 100° or in a vacuum exsiccator at room temperature. The 0.1 molar solution colors methyl red a transition shade.

Borax: The thrice recrystallized commercial preparation is dried to constant weight in an exsiccator over deliquescent sodium bromide. The composition is then $Na_2B_4O_710H_2O$; the $\frac{1}{20}$ molar solution contains 19.10 g. per liter.

Sodium Carbonate: Most simply obtained pure by heating sodium bicarbonate or oxalate for half an hour at 360° (Lunge (11), Sörensen (11)).

Glycocoll (Kahlbaum): A solution of 2 g. of glycocoll in 20 cc. of water should remain clear and should give no precipitate with barium nitrate; with silver nitrate at most a slight opalescence. The ash of 5 g. of glycocoll should not amount to more than 2 mg. The nitrogen content, determined according to Kjeldahl, should be 18.67 ± 0.1 per cent.

Citric Acid (Kahlbaum): A commercial preparation may be used after twice recrystallizing from water and drying over sodium bromide to constant weight. The composition is then $C_6H_8O_7H_2O$.

According to Sörensen the acid should give a clear solution that gives no reaction with barium or silver nitrate. The ash from 5 g. should be less than 1 mg. The acid loses its water

of crystallization when dried at 70° and 20–30 mm. Per cent loss in weight: 8.58 ± 0.1 %.

The solution of secondary citrate is prepared from citric acid: 21.01 g. of citric acid are dissolved in 200 cc. N sodium hydroxide and diluted to 1 liter.

Borax Solution according to Sörensen (2): 12.40 g. boric acid are dissolved in 100 cc. N sodium hydroxide and diluted to 1 liter. It is better to start with pure borax and make an 0.05 molar solution from this preparation (19.10 g. in a liter).

Succinic Acid: The high-grade commercial material may be purified by two or three recrystallizations from distilled water. It should be dried in air in thin layers and finally to constant weight in a desiccator over calcium chloride. There is no water of crystallization. The acid must not be dried at high temperature for two molecules lose one of water to form the anhydride of the acid. A stock solution can not be preserved well because it soon becomes mouldy. The addition of a little thymol tends to preserve it. The 0.05 molar solution contains 5.90 g. of acid per liter of solution.

A summary of the various buffer mixtures and their hydrogen exponents is given in the following tables. The most suitable indicators are given in the last columns. The mixtures given in italics no longer show good buffering action.

$\frac{1}{5}$ Mol. HCl + $\frac{1}{5}$ Mol. KCl (Clark and Lubs (5))

Composition	p_H	Indicator
97.0 cc. HCl+50 cc. KCl dil. to 200 cc.	1.0	Thymol blue, Tropeolin 00
64.5 cc. HCl+50 cc. KCl dil. to 200 cc.	1.2	
41.5 cc. HCl+50 cc. KCl dil. to 200 cc.	1.4	
26.3 cc. HCl+50 cc. KCl dil. to 200 cc.	1.6	
16.6 cc. HCl+50 cc. KCl dil. to 200 cc.	1.8	
10.6 cc. HCl+50 cc. KCl dil. to 200 cc.	2.0	
6.7 cc. HCl+50 cc. KCl dil. to 200 cc.	2.2	

$\frac{1}{10}$ Mol. Potass. Biphthalate + $\frac{1}{10}$ Mol. HCl (Clark and Lubs (5))

Composition	p_H	Indicator
46.70 cc. HCl+50 cc. biphthalate to 100 cc.	2.2	Tropeolin 00 Thymol blue.
39.60 cc. HCl+50 cc. biphthalate to 100 cc.	2.4	
32.95 cc. HCl+50 cc. biphthalate to 100 cc.	2.6	
26.42 cc. HCl+50 cc. biphthalate to 100 cc.	2.8	
20.32 cc. HCl+50 cc. biphthalate to 100 cc.	3.0	Methyl orange, Brom phenol blue.
14.70 cc. HCl+50 cc. biphthalate to 100 cc.	3.2	
9.90 cc. HCl+50 cc. biphthalate to 100 cc.	3.4	
5.97 cc. HCl+50 cc. biphthalate to 100 cc.	3.6	
2.63 cc. HCl+50 cc. biphthalate to 100 cc.	3.8	

$\frac{1}{10}$ Mol. Potass. Biphthalate + $\frac{1}{10}$ Mol. NaOH (Clark and Lubs (5))

Composition	p_H	Indicator
0.40 cc. NaOH+50 cc. biphthalate to 100 cc.	4.0	Methyl orange, Brom phenol blue.
3.70 cc. NaOH+50 cc. biphthalate to 100 cc.	4.2	
7.50 cc. NaOH+50 cc. biphthalate to 100 cc.	4.4	
12.15 cc. NaOH+50 cc. biphthalate to 100 cc.	4.6	
17.70 cc. NaOH+50 cc. biphthalate to 100 cc.	4.8	
23.85 cc. NaOH+50 cc. biphthalate to 100 cc.	5.0	Methyl red, Brom cresol purple.
29.95 cc. NaOH+50 cc. biphthalate to 100 cc.	5.2	
35.45 cc. NaOH+50 cc. biphthalate to 100 cc.	5.4	
39.85 cc. NaOH+50 cc. biphthalate to 100 cc.	5.6	
43.00 cc. NaOH+50 cc. biphthalate to 100 cc.	*5.8*	
45.45 cc. NaOH+50 cc. biphthalate to 100 cc.	*6.0*	
47.00 cc. NaOH+50 cc. biphthalate to 100 cc.	*6.2*	

$\frac{1}{10}$ Mol. Biphosphate + $\frac{1}{10}$ Mol. NaOH Dil. to 100 cc. (Clark and Lubs (5))

Composition	p_H	Indicator
3.72 cc. NaOH+50 cc. phosphate dil. 100 cc.	*5.8*	Methyl red, Brom cresol purple, Brom thymol blue.
5.70 cc. NaOH+50 cc. phosphate dil. 100 cc.	*6.0*	
8.60 cc. NaOH+50 cc. phosphate dil. 100 cc.	6.2	
12.60 cc. NaOH+50 cc. phosphate dil. 100 cc.	6.4	
17.80 cc. NaOH+50 cc. phosphate dil. 100 cc.	6.6	
23.65 cc. NaOH+50 cc. phosphate dil. 100 cc.	6.8	Neutral red, Phenol red, Cresol red.
29.63 cc. NaOH+50 cc. phosphate dil. 100 cc.	7.0	
35.00 cc. NaOH+50 cc. phosphate dil. 100 cc.	7.2	
39.50 cc. NaOH+50 cc. phosphate dil. 100 cc.	7.4	
42.80 cc. NaOH+50 cc. phosphate dil. 100 cc.	7.6	
45.20 cc. NaOH+50 cc. phosphate dil. 100 cc.	*7.8*	
46.80 cc. NaOH+50 cc. phosphate dil. 100 cc.	*8.0*	

$\frac{1}{10}$ Mol. Boric Acid in $\frac{1}{10}$ Mol. KCl + $\frac{1}{10}$ Mol. NaOH Dil. to 100 cc. (Clark and Lubs (5))

Composition	p_H	Indicator
2.61 cc. NaOH+50 cc. boric acid dil. 100 cc.	*7.8*	
3.97 cc. NaOH+50 cc. boric acid dil. 100 cc.	*8.0*	Cresol red.
5.90 cc. NaOH+50 cc. boric acid dil. 100 cc.	8.2	Phenol phthalein, Thymol blue.
8.50 cc. NaOH+50 cc. boric acid dil. 100 cc.	8.4	
12.00 cc. NaOH+50 cc. boric acid dil. 100 cc.	8.6	
16.30 cc. NaOH+50 cc. boric acid dil. 100 cc.	8.8	
21.30 cc. NaOH+50 cc. boric acid dil. 100 cc.	9.0	
26.70 cc. NaOH+50 cc. boric acid dil. 100 cc.	9.2	
32.00 cc. NaOH+50 cc. boric acid dil. 100 cc.	9.4	
36.85 cc. NaOH+50 cc. boric acid dil. 100 cc.	9.6	
40.80 cc. NaOH+50 cc. boric acid dil. 100 cc.	9.8	
43.90 cc. NaOH+50 cc. boric acid dil. 100 cc.	10.0	Thymol phthalein.

$\frac{1}{15}$ MOL. NaH_2PO_4 + AND $\frac{1}{10}$ MOL. Na_2HPO_4 (SÖRENSEN (2))

Composition	p_H at 18°
9.75 cc. NaH_2PO_4+0.25 cc. Na_2HPO_4	*5.29*
9.5 cc. NaH_2PO_4+0.5 cc. Na_2HPO_4	*5.59*
9.0 cc. NaH_2PO_4+1.0 cc. Na_2HPO_4	5.91
8.0 cc. NaH_2PO_4+2.0 cc. Na_2HPO_4	6.24
7.0 cc. NaH_2PO_4+3.0 cc. Na_2HPO_4	6.47
6.0 cc. NaH_2PO_4+4.0 cc. Na_2HPO_4	6.64
5.0 cc. NaH_2PO_4+5.0 cc. Na_2HPO_4	6.81
4.0 cc. NaH_2PO_4+6.0 cc. Na_2HPO_4	6.98
3.0 cc. NaH_2PO_4+7.0 cc. Na_2HPO_4	7.17
2.0 cc. NaH_2PO_4+8.0 cc. Na_2HPO_4	7.38
1.0 cc. NaH_2PO_4+9.0 cc. Na_2HPO_4	7.73
0.5 cc. NaH_2PO_4+9.5 cc. Na_2HPO_4	8.04

$\frac{1}{20}$ MOL. BORAX WITH 0.1 N HCL (SÖRENSEN (2))

Composition	p_H At			
	18°	10°	40°	70°
	(Sörensen)	(Walbum)		
5.25 cc. borax+4.75 cc. HCl	*7.62*	*7.64*	*7.55*	*7.47*
5.5 cc. borax+4.5 cc. HCl	7.94	7.96	7.86	7.76
5.75 cc. borax+4.25 cc. HCl	8.14	8.17	8.06	7.95
6.0 cc. borax+4.0 cc. HCl	8.29	8.32	8.19	8.08
6.5 cc. borax+3.5 cc. HCl	8.51	8.54	8.40	8.26
7.0 cc. borax+3.0 cc. HCl	8.68	8.72	8.56	8.40
7.5 cc. borax+2.5 cc. HCl	8.80	8.84	8.67	8.50
8.0 cc. borax+2.0 cc. HCl	8.91	8.96	8.77	8.59
8.5 cc. borax+1.5 cc. HCl	9.01	9.06	8.86	8.67
9.0 cc. borax+1.0 cc. HCl	9.09	9.14	8.94	8.74
9.5 cc. borax+0.5 cc. HCl	9.17	9.22	9.01	8.80
10.0 cc. borax+0.0 cc. HCl	9.24	9.30	9.08	8.86

$\frac{1}{20}$ MOL. BORAX WITH 0.1 N NaOH (SÖRENSEN (2))

Composition	p_H At			
	18°	10°	40°	70°
	(Sörensen)	(Walbum)		
10.0 cc. borax+0.0 cc. NaOH	9.24	9.30	9.08	8.86
9 cc. borax+1 cc. NaOH	9.36	9.42	9.18	8.94
8 cc. borax+2 cc. NaOH	9.50	9.57	9.30	9.02
7 cc. borax+3 cc. NaOH	9.68	9.76	9.44	9.12
6 cc. borax+4 cc. NaOH	9.97	10.06	9.67	9.28
5 cc. borax+5 cc. NaOH	*11.07*	*11.24*	*10.61*	*9.98*

0.1 MOL. GLYCOCOLL (THAT CONTAINS 0.1 N NaCl) AND 0.1 N HCl (SÖRENSEN (2)

Composition	p_H at 18° (Sörensen)
0.0 cc. glycocoll+10 cc. HCl	1.04
1.0 cc. glycocoll+ 9 cc. HCl	1.15
2 cc. glycocoll+ 8 cc. HCl	1.25
3 cc. glycocoll+ 7 cc. HCl	1.42
4 cc. glycocoll+ 6 cc. HCl	1.645
5 cc. glycocoll+ 5 cc. HCl	1.93
6 cc. glycocoll+ 4 cc. HCl	2.28
7.0 cc. glycocoll+ 3 cc. HCl	2.61
8 cc. glycocoll+ 2 cc. HCl	2.92
9 cc. glycocoll+ 1 cc. HCl	3.34
9.5 cc. glycocoll+ 0.5 cc. HCl	3.68

0.1 Mol. Sec. Citrate and 0.1 N HCl (Sörensen (2))

Composition	p_H at 18° (Sörensen)
0.0 cc. citrate +10 cc. HCl	*1.04*
1.0 cc. citrate + 9 cc. HCl	*1.17*
2.0 cc. citrate + 8 cc. HCl	*1.42*
3.0 cc. citrate + 7 cc. HCl	*1.925*
3.33 cc. citrate + 6.67 cc. HCl	*2.27*
4.0 cc. citrate + 6 cc. HCl	*2.97*
4.5 cc. citrate + 5.5 cc. HCl	*3.36*
4.75 cc. citrate+ 5.25 cc. HCl	3.53
5 cc. citrate+ 5 cc. HCl	3.69
5.5 cc. citrate+ 4.5 cc. HCl	3.95
6.0 cc. citrate+ 4 cc. HCl	4.16
7.0 cc. citrate+ 3 cc. HCl	4.45
8.0 cc. citrate+ 2 cc. HCl	4.65
9.0 cc. citrate+ 1 cc. HCl	4.83
9.5 cc. citrate+ 0.5 cc. HCl	4.89
10.0 cc. citrate+ 0.0 cc. HCl	4.96

0.1 Mol. Sec. Citrate with 0.1 N NaOH (Sörensen (2))

Composition	p_H at 18° (Sörensen)	p_H at 10° (Walbum)	p_H at 40° (Walbum)	p_H at 70° (Walbum)
10.0 cc. citrate 0.0 cc. NaOH	4.96	4.93	5.04	5.14
9.5 cc. citrate 0.5 cc. NaOH	5.02	4.99	5.10	5.20
9.0 cc. citrate 1.0 cc. NaOH	5.11	5.08	5.19	5.29
8.0 cc. citrate 2.0 cc. NaOH	5.31	5.27	5.39	5.49
7.0 cc. citrate 3.0 cc. NaOH	5.57	5.53	5.64	5.75
6.0 cc. citrate 4.0 cc. NaOH	5.97	5.94	6.04	6.15
5.5 cc. citrate 4.5 cc. NaOH	*6.33*	*6.30*	*6.41*	*6.51*

0.1 Mol. Glycocoll (Containing 0.1 N NaCl) and 0.1 N NaOH (Sörensen (2))

Composition	p_H at 18° (Sörensen)	10° (Walbum)	40° (Walbum)	70° (Walbum)
9.75 cc. glycocoll 0.25 cc. NaOH	8.24			
9.5 cc. glycocoll 0.5 cc. NaOH	8.575	8.75	8.12	7.48
9.0 cc. glycocoll 1.0 cc. NaOH	8.93	9.10	8.45	7.79
8.0 cc. glycocoll 2.0 cc. NaOH	9.36	9.54	8.85	8.16
7.0 cc. glycocoll 3.0 cc. NaOH	9.71	9.90	9.18	8.45
6.0 cc. glycocoll 4.0 cc. NaOH	10.14	10.34	9.58	8.82

$\frac{1}{5}$ Mol. Boric Acid and $\frac{1}{20}$ Mol. Borax (Palitzsch (4))

0.3 cc. borax+9.7 cc. boric acid	*6.77*	Neutral red, phenol red, Cresol red.
0.6 cc. borax+9.4 cc. boric acid	*7.09*	
1.0 cc. borax+9.0 cc. boric acid	*7.36*	
1.5 cc. borax+8.5 cc. boric acid	7.60	
2.0 cc. borax+8.0 cc. boric acid	7.78	
2.5 cc. borax+7.5 cc. boric acid	7.94	
3.0 cc. borax+7.0 cc. boric acid	8.08	
3.5 cc. borax+6.5 cc. boric acid	8.20	Phenol phthalein. Thymol blue.
4.5 cc. borax+5.5 cc. boric acid	8.41	
5.5 cc. borax+4.5 cc. boric acid	8.60	
6.0 cc. borax+4.0 cc. boric acid	8.69	
7.0 cc. borax+3.0 cc. boric acid	8.84	
8.0 cc. borax+2.0 cc. boric acid	8.98	
9.0 cc. borax+1.0 cc. boric acid	9.11	
10.0 cc. borax+0.0 cc. boric acid	9.24	

0.05 Mol. Borax and 0.1 Mol. NaOH (Sörensen (2))

9 cc. borax+1 cc. NaOH	9.36	Thymol phthalein.
8 cc. borax+2 cc. NaOH	9.50	
7 cc. borax+3 cc. NaOH	9.68	
6 cc. borax+4 cc. NaOH	9.97	
5 cc. borax+5 cc. NaOH	*11.07*	
4 cc. borax+6 cc. NaOH	*12.37*	

0.1 MOL. Na_2CO_3 AND 0.1 MOL. HCl (KOLTHOFF)

20 cc. HCl+50 cc. Na_2CO_3 to 100	10.17	Thymol phthalein.
15 cc. HCl+50 cc. Na_2CO_3 to 100	10.35	
10 cc. HCl+50 cc. Na_2CO_3 to 100	10.55	
5 cc. HCl+50 cc. Na_2CO_3 to 100	10.86	Alizarine yellow, Nitramin, Tropeolin 0.
3 cc. HCl+50 cc. Na_2CO_3 to 100	11.04	
0 cc. HCl+50 cc. Na_2CO_3 to 100	11.36	

0.05 MOL. Na_2HPO_4 AND 0.1 MOL. NaOH (SÖRENSEN)

	p_H
9 cc. Na_2HPO_4+1 cc. NaOH	11.22
6.67 cc. Na_2HPO_4+3.33 cc. NaOH	12.12

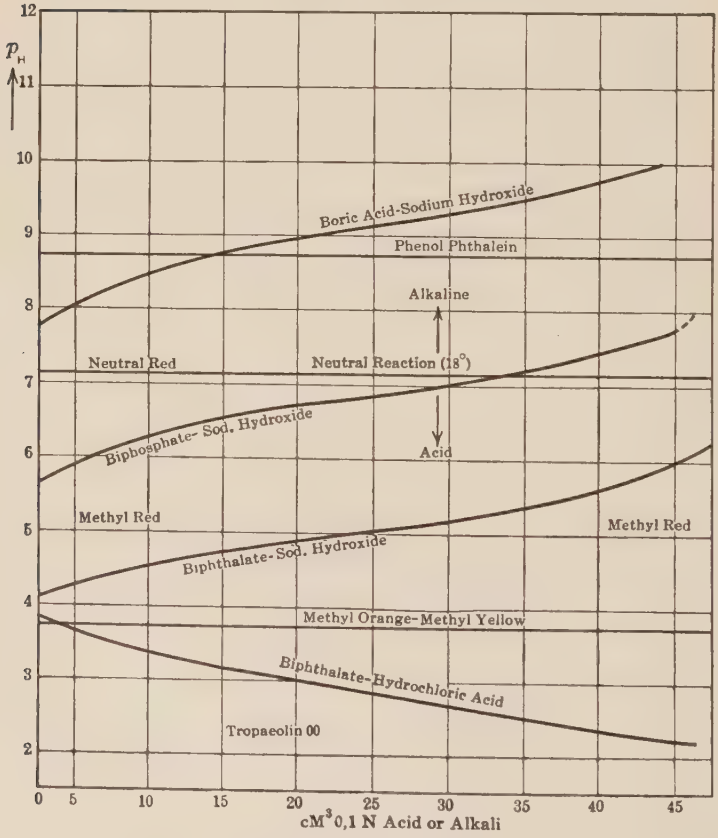

FIG. 17.—Buffer mixtures of Clark and Lubs.

0.15 Mol. Na_2HPO_4 and 0.1 Mol. NaOH (Ringer (8))

15 cc. NaOH+50 cc. Na_2HPO_4	10.97	
25 cc. NaOH+50 cc. Na_2HPO_4	11.29	Tropeolin 0,
50 cc. NaOH+50 cc. Na_2HPO_4	11.77	Alizarine yellow,
75 cc. NaOH+50 cc. Na_2HPO_4	12.06	Nitramin.

A new set of buffer mixtures that can be prepared without the use of standard acid or base has been proposed by the author (12). Weighed salts or acids are used, so that the preparation of standard acid or base is not necessary. These statements apply to mixtures of succinic acid and borax, which furnish buffers of p_H 3.0 to 5.8, while primary phosphate—borax mixtures give a range of p_H from 6.0 to 9.2.

0.05 Mol. Succinic Acid and 0.05 Mol. Borax (Kolthoff (12))

Composition	p_H at 18°
9.86 cc. succinic acid+0.14 cc. borax	3.0
9.65 cc. succinic acid+0.35 cc. borax	3.2
9.40 cc. succinic acid+0.60 cc. borax	3.4
9.05 cc. succinic acid+0.95 cc. borax	3.6
8.63 cc. succinic acid+1.37 cc. borax	3.8
8.22 cc. succinic acid+1.78 cc. borax	4.0
7.78 cc. succinic acid+2.22 cc. borax	4.2
7.38 cc. succinic acid+2.62 cc. borax	4.4
7.00 cc. succinic acid+3.00 cc. borax	4.6
6.65 cc. succinic acid+3.35 cc. borax	4.8
6.32 cc. succinic acid+3.68 cc. borax	5.0
6.05 cc. succinic acid+3.95 cc. borax	5.2
5.79 cc. succinic acid+4.21 cc. borax	5.4
5.57 cc. succinic acid+4.43 cc. borax	5.6
5.40 cc. succinic acid+4.60 cc. borax	5.8

0.1 Mol. KH_2PO_4 + 0.05 Mol. Borax (Kolthoff (12))

Composition	p_H at 18°
9.21 cc. KH_2PO_4+0.79 cc. borax	5.8
8.77 cc. KH_2PO_4+1.23 cc. borax	6.0
8.30 cc. KH_2PO_4+1.70 cc. borax	6.2
7.78 cc. KH_2PO_4+2.22 cc. borax	6.4
7.22 cc. KH_2PO_4+2.78 cc. borax	6.6
6.67 cc. KH_2PO_4+3.33 cc. borax	6.8
6.23 cc. KH_2PO_4+3.77 cc. borax	7.0
5.81 cc. KH_2PO_4+4.19 cc. borax	7.2
5.50 cc. KH_2PO_4+4.50 cc. borax	7.4
5.17 cc. KH_2PO_4+4.83 cc. borax	7.6
4.92 cc. KH_2PO_4+5.08 cc. borax	7.8
4.65 cc. KH_2PO_4+5.35 cc. borax	8.0
4.30 cc. KH_2PO_4+5.70 cc. borax	8.2
3.87 cc. KH_2PO_4+6.13 cc. borax	8.4
3.40 cc. KH_2PO_4+6.60 cc. borax	8.6
2.76 cc. KH_2PO_4+7.24 cc. borax	8.8
1.75 cc. KH_2PO_4+8.25 cc. borax	9.0
0.50 cc. KH_2PO_4+9.50 cc. borax	9.2

If a mixture of higher p_H (than 12) is to be used, it is most convenient to dilute 0.1 or 1.0 N NaOH with carbonate-free water to an appropriate extent. The $[OH^-]$, $[H^+]$, and p_H may be calculated from the degree of dissociation. The Clark and Lubs solutions of biphthalate mixed with hydrochloric acid or sodium hydroxide are made from $\frac{1}{5}$ N solutions, according to their directions. Since N/5 solutions of HCl and NaOH are not usually on hand, equivalent amounts of 0.1 N solution may be used, as the author has directed in the tables. Certain of the mixtures were compared with those prepared by Clark and Lubs specifications at 18° using the hydrogen electrode; no greater difference than 0.05 in p_H was found.

The dependence of buffer capacity on composition can easily be derived by the considerations of Van Slyke (p. 24). The author has indicated the molecular buffer capacities of Clark's phosphate mixtures at various p_H values in Fig. 18.

The investigators quoted made their H-ion determinations with the hydrogen electrode at 18 or 25°. The p_H of the mixtures varies only slightly with changing temperature. On the

contrary, mixtures of ammonia and ammonium chloride, whose p_H Hildebrand (13) and Blum (14) have shown to be strongly influenced by temperature, are not to be recommended.

McIlvaine (15) has determined the hydrogen exponents of mixtures of 0.2 molar secondary sodium phosphate and 0.1 molar citric acid. In the region of the point that corresponds to the reaction of primary phosphate the liquid has a good buffering action (*cf.* Van Slyke, page 24). It would be desirable to have the p_H-values of McIlvaine's solutions redetermined on dilute solutions, since the salt error may play a very large rôle at the concentrations of his solutions.

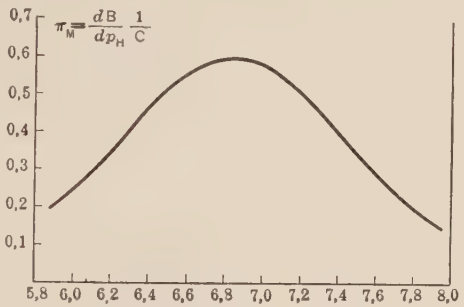

FIG. 18.—Molecular buffer capacities of Clark's phosphate solutions.

MIXTURES OF 0.2 MOL. CITRIC ACID WITH 0.2 MOL. SECONDARY SODIUM PHOSPHATE (MCILVAINE (15))

0.1 Mol. Citric Acid, cc.	0.2 Mol. Na_2HPO_4, cc.	p_H	0.1 Mol. Citric Acid, cc.	0.2 Mol. Na_2HPO_4, cc.	p_H
19.60	0.40	2.2	9.28	10.72	5.2
18.76	1.24	2.4	8.85	11.15	5.4
17.82	2.18	2.6	8.40	11.60	5.6
16.83	3.17	2.8	7.91	12.09	5.8
15.89	4.11	3.0	7.37	12.63	6.0
15.06	4.94	3.2	6.78	13.22	6.2
14.30	5.70	3.4	6.15	13.85	6.4
13.56	6.44	3.6	5.45	14.55	6.6
12.90	7.10	3.8	4.55	15.45	6.8
12.29	7.71	4.0	3.63	16.37	7.0
11.72	8.28	4.2	2.61	17.39	7.2
11.18	8.82	4.4	1.83	18.17	7.4
10.65	9.35	4.6	1.27	18.73	7.6
10.14	9.86	4.8	0.85	19.15	7.8
9.70	10.30	5.0	0.55	19.45	8.0

Acree, Millon, Avery, and Slagle (15) have selected the following mixture as a general buffer solution:

1 molar primary potassium phosphate.
$\frac{5}{8}$ molar sodium formate,
$\frac{3}{8}$ molar sodium acetate,
1 molar sodium phenolsuphonate,
1 molar secondary phosphate,
0.005 molar thymol (saturated solution).

The solution is brought to the desired p_H by addition of 0.5 mol. HCl or NaOH; the p_H values are derived from a graph.

Then 10 cc. of the solution are diluted to twice their volume.

E. B. R. Prideaux and A. T. Ward (16) use a mixture of acids in preparing a "universal buffer solution," with a p_H range between 2 and 12. The mixture consists of equivalent amounts of phosphoric, phenyl acetic, and boric acids. A 0.1 N solution is made and partially neutralized with 0.1 sodium hydroxide.

Per Cent Neutralized	p_H	Per Cent Neutralized	p_H
0	1.99	55	
5	2.13	60	7.91
10		65	8.62
15	2.65	70	9.11
20	3.10	75	
25	3.73	80	10.21
30	4.21	85	
35	4.80	90	11.41
40	5.43	95	
45	6.30	100	11.94
50	6.84		

3. Technique of the Determination.—It must be clear as to which indicator is most suitable. The reaction of the liquid is tested by various indicator papers, as congo, litmus, or phenol phthalein paper, or small amounts of the liquid are tested with different indicators. Having found roughly that a solution is acid to phenol phthalein and weakly alkaline to litmus, and must therefore have a p_H in the neighborhood of 7–8, neutral red would probably be satisfactory for the determination. A suitable

reference solution is then selected. For the actually determination colorless test-tubes of Jena, Cologne-Ehrenfeld, or Pyrex glass, and of *as nearly as possible the same diameter*, are used.

(If only a small amount of fluid is available, Felton's (17) procedure may be used, namely, place a drop of the liquid on a porcelain plate (spot plate), add a drop of indicator and compare the color with that of a drop of buffer solution treated in the same manner. For micro-colorimetric determinations see V. C. Myers, H. W. Schmitz, and L. L. Booker (17); J. H. Brown (17).)

To every 10 cc. of solution is added some indicator,—about a drop of solution of the concentration given in Chapter III,—and the reference solution is treated in exactly the same manner. It is best to use a test-tube stand during the comparison of the colors; the tubes are supported obliquely at an angle of 35–40° to the vertical, against a white background of milky glass, or paper. The colors may now be judged in two different ways. One consists in looking through the tubes toward a bright background. Another way is to look up from below, the stand being turned through an angle of 35–40°. Enough reference solutions must be prepared so that the color of the unknown falls between two of those of the series, and not beyond. Furthermore, *the unknown and the reference solution must have equal quantities* (exactly measured) *of the same indicator*. The concentration is of very great significance if the indicator is one-colored. With two-colored indicators it is not as important, since the ratio of the acid and alkaline forms is judged. Here too it is advantageous to add the indicator with a small pipette rather than with a dropping bottle. Differences between various colorimetric determinations with phenol phthalein have been traced back to the fact that the indicator was added from a dropping bottle in some instances. The same holds true for thymol phthalein, *p*-nitro-phenol, nitramin, etc.

It is also important that the unknown and reference solutions be treated simultaneously with indicator and observed after standing a short time. The color intensity of some indicators decreases on standing. Methyl violet is green in 0.1 N HCl.

After fifteen minutes the color has decreased markedly, and disappears after an hour. It is therefore advantageous to observe and compare rapidly after the indicator has been added. Here again circumstances are favorable, for the speed of decomposition of the indicator depends upon the hydrogen-ion concentration, and therefore goes at the same rate in both solutions. The color must also be observed quickly in case of the slightly-soluble indicators, because there is the possibility that an excess of such an indicator may remain in colloidal solution for a time and then separate in flocculent form. A part of the dissolved indicator may be absorbed by the flocculent precipitate, thus making the color erratic. If, for example, a drop of 0.1 per cent methyl yellow solution is added to 10 cc. of a primary phosphate solution and the color observed at once, and then after fifteen minutes, it can be plainly seen that the color has faded on standing, since most of the indicator has separated out. The azo-compounds that are insoluble in water are especially apt to behave in this way. The water-soluble ones, however, such as methyl orange and tropeolin 00, give a color that is constant for several days. Nevertheless it is not advisable to prepare reference solutions treated with indicator in advance, because almost all indicators change their color on standing (especially in sunlight). The color of the alkaline solutions of many indicators is unstable. Phenol and thymol phthaleins are gradually transformed into colorless carbonic acids. The red-brown color of the very acid-sensitive nitramin disappears when the strongly alkaline solution is allowed to stand.

A disadvantage of the Clark and Lubs sulphone phthaleins with their brilliant transition colors is that some of them show marked dichromatism in their transition range, especially brom phenol blue and brom cresol purple. An improvement results from the use of the new indicators, chlor phenol red and brom cresol blue, that Barnett Cohen developed. The details of this phenomenon have been extensively discussed in the third chapter (pages 73 ff). In general, indicators with a small interval give the best results in colorimetric determinations. The color changes for small changes of hydrogen-ion concentration are much sharper than when the interval is more extended. Although

a smaller number of indicators needs to be on hand for the measurement of any p_H if those of wider transition intervals are used, none the less it is better to use only indicators with small intervals. The total number of indicators that is necessary to carry out the determination of any p_H that may be in question is greater; but at the same time the accuracy of the individual determinations is higher. Litmus or azolitmin has a range of about 5–8, and neutral red and phenol red of 6.8–8.0. Both may thus be used for p_H-values between 6.8 and 8.0, but the change is much sharper in case of phenol red or neutral red. In general the accuracy of determination is about 0.1 p_H-unit. In very exact work, with comparison solutions that differ by 0.1 p_H-unit, and with suitable indicators, the value may be found to 0.05 p_H. Higher accuracy is scarcely to be attained since electrolytes, etc., present in the solutions influence the color. As may be seen from Fig. 11, Chapter III (page 57), the absolute color change of an indicator for small changes in hydrogen-ion concentration is greatest when p_H is approximately equal to p_{HIn}. Hence in colorimetric determinations that indicator will give the most exact p_H-value whose p_{HIn} is equal to the p_H of the solution, i.e., the p_H to be found must lie about in the middle of the transition interval of the indicator. If the p_H lies nearer the end of the interval the color is, in general, less sharply matched. This applies especially to the two-color indicators, since in one-color indicators we are not judging between the relative amounts of two forms, but the absolute amount of a single form. The maximum accuracy in case of the sulphone phthaleins does not lie at $p_H = p_{HIn}$, but at the beginning of the transition interval. According to J. T. Saunders (18) the following indicators give results of accuracy 0.01 to 0.02 p_H in the p_H-range mentioned:

	p_H Range:
Brom cresol purple	5.80–6.40
Brom thymol blue	6.40–7.20
Phenol red	7.10–7.90
Cresol red	7.65–8.45
Thymol blue	8.40–9.20

The reason for the displacement of the maximum sensitivity is that the alkaline color is more intense than the yellow acid form.

A small amount of the alkaline form is therefore very readily perceptible in presence of the acid.

4. Measurements Without Buffer Mixtures.—L. J. Gillespie (19) proposed a simplification of the colorimetric procedure that avoids the use of buffer mixtures and uses simply two tubes of equal diameter in one of which a certain number of drops of pure acid form of the indicator are placed, in the other enough of the alkaline to bring the total up to ten drops of indicator. A series of comparison tints is established in this way. The material to be examined is treated with ten drops of the same indicator and compared with the two other tubes, one of which is placed behind the other. To obtain good optical comparison it is well to place a tube with the same volume of water behind that containing the solution under examination. The author deems it more convenient to use small cylinders or cells, that can be placed behind each other, instead of test-tubes. The principle of the procedure is very simple. Every transition tint between acid and alkaline color corresponds to a certain p_H. By changing the number of drops in the two tubes the total transition interval of the indicator may be run through. Thus, for methyl red, for example:

1 drop alkaline and 9 drops acid correspond to $p_H = 4.05$
5 drops alkaline and 5 drops acid correspond to $p_H = 5.0$
9 drops alkaline and 1 drop acid correspond to $p_H = 5.95$.

Later Gillespie (19) gave an extensive exposition of his procedure. According to his view one may tacitly use the following practical equation:

$$p_H = p_{HIn} + \log \text{ “drop ratio.”}$$

Gillespie using aqueous indicator solutions found the following values of p_{HIn} at the temperature given:

Indicator	B. P. B.	M. R.	B. C. P.	P. R.	C. R.	T. B.
Temperature	31°	30°	30°	29°	24°	24°
p_{HIn}	4.06	4.96	6.26	7.72	8.08	8.82
Strength of Indicator solution, per cent	0.008	0.003	0.012	0.004	0.008	0.008

The following table may be used in the determination of p_H with various indicators:

Drop Ratio, Acid/Alkali	p_H for Each Pair of Tubes						
	B.P.B.	M. R.	B.C.P.	B.T.B.	P. R.	C. R.	T. B.
1 : 9	3.1	4.05	5.3	6.15	6.75	7.15	7.85
1.5 : 8.5	3.3	4.25	5.5	6.35	6.95	7.35	8.05
2 : 8	3.5	4.4	5.7	6.5	7.1	7.5	8.2
3 : 7	3.7	4.6	5.9	6.7	7.3	7.7	8.4
4 : 6	3.9	4.8	6.1	6.9	7.5	7.9	8.6
5 : 5	4.1	5.0	6.3	7.1	7.7	8.1	8.8
6 : 4	4.3	5.2	6.5	7.3	7.9	8.3	9.0
7 : 3	4.5	5.4	6.7	7.5	8.1	8.5	9.2
8 : 2	4.7	5.6	6.9	7.7	8.3	8.7	9.4
8.5 : 1.5	4.8	5.75	7.0	7.85	8.45	8.85	9.55
9 : 1	5.0	5.95	7.2	8.05	8.65	9.05	9.75
Per cent indicator solution	0.008	0.008	0.012	0.008	0.004	0.008	0.00
Cc. 0.1 N NaOH per 0.1 g. indicator	1.64	.....	2.78	1.77	3.10	2.88	2.388
Acid color established with HCl	0.05 N	0.05 N	0.05 N	0.05 N	0.05 N	2% KH_2PO_4	2% KH_2PO_4
Quantity of acid to establish acid color of 10 cc. of solution	1 cc.	1 drop	1 drop	1 drop	1 drop	1 drop	1 drop

B. P. B. = brom phenol blue. M. R. = methyl red. B. C. P. = brom cresol purple. B. T. B. = brom thymol blue. P. R. = phenol red. C.R. = cresol red. T.B. = thymol blue.

Gillespie used tubes 1.5 × 15 cm. for the determinations. The two tubes containing the total of 10 drops of indicator are always placed one behind the other. In one tube the indicator has its full acid, in the other its full alkaline color.

Equal volumes of liquid are added to all of the tubes, i.e., 5–6 cc. Ten drops of indicator solution are added to the solution to be tested, and the tubes are placed in the so-called comparator (*cf.* Fig. 19).

W. D. Hatfield (19) gives a slight modification of Gillespie's method. Instead of producing the standard colors with strong acids and bases as Gillespie does, Hatfield recommends the use

of weak acids or bases. The colored solutions thus obtained may be kept for a much longer time,—most of them from 4 to 8 weeks. Mixtures that contain methyl red deteriorate rapidly, however. Hatfield recommends:

1 : N acetic acid for brom phenol blue and methyl red.

2 : 7.0 g. KH_2PO_4 per liter to develop the acid colors of brom cresol purple, brom thymol blue, phenol red, cresol red, and thymol blue (yellow color).

3 : 18 g. $Na_2HPO_412H_2O$ per liter for the alkaline colors of brom phenol blue, methyl red, brom cresol purple, and brom thymol blue.

4 : 1.0 g. Na_2CO_3 per liter for the alkaline color of brom cresol purple, brom thymol blue, phenol red, cresol red, and thymol blue.

In another communication Gillespie (19) describes a simple colorimeter that may be used in the determination. Although the basis upon which it operates is simple, it seems to the author of little practical use.

A and C are fixed. B moves along a graduated scale which is read by a pointer on B. The pointer may move over 100 scale divisions. The acidified indicator solution of suitable strength may be placed in B, the alkaline solution of equal strength in C. The solution to be examined, if colored or turbid, is received in the small tube A. In this case an amount of water equal to that of the solution is placed in D.

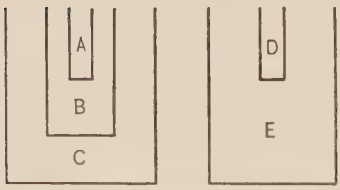

FIG. 19.—Gillespie's colorimeter.

The solution to be examined is placed in E, and enough indicator to make the concentration the same as in B and C. B is then moved until the colors are matched, and the scale reading then gives the ratio of the acid to the alkaline color.

Ernest van Alvine (20) uses the same principle as Gillespie, but employs a different colorimeter. He also gives a curve with ratio acid to alkaline form $\left(\text{or } \frac{\alpha}{1-\alpha}\right)$ as ordinate, while

the abscissa-axis gives the corresponding p_H for the various indicators. If p_{HIn} is known these values may be calculated directly:

$$p_H = p_{HIn} + \log \frac{\alpha}{1 - \alpha}.$$

The procedure of Michaelis using one-color indicators that is later to be described also rests on this principle.

The curve of van Alvine is given here (Fig. 20) because it enables us to read off the p_H for various indicators without further calculation.

EXAMPLE.— $\frac{\alpha}{1 - \alpha} = 38.7$; then:

p_H using thymol blue is	2.9 (Change in acid solution)
p_H using thymol blue is	8.8 (Change in alkaline solution)
p_H using brom phenol blue is	3.9
p_H using methyl red is	5.3
p_H using brom cresol purple is	6.1

The author notes here that neither Gillespie nor van Alvine have given a direct proof that the equation:

$$p_H = p_{HIn} + \log \frac{\alpha}{1 - \alpha},$$

which only holds for monobasic indicators, may also be used for the dibasic phenol sulphone phthaleins. Recently Kolthoff (21) has shown that the equation is also valid in these cases.

Bjerrum has used the principle of the procedure in the determination of the dissociation constants of indicators. The author (39) has also used it in determining the hydrogen exponent of drinking water using neutral red as indicator. Two wedges that could be tightly closed were selected; they were cemented together with Canada balsam. One wedge was filled with a 0.5 : 100,000 solution of neutral red in 0.1 N acetic acid, and the other with a 1 : 100,000 solution of the indicator in approximately 0.1 N ammonia with 50 per cent glycerine which is added to prevent the flocking out of the indicator. On one side of this simple apparatus are placed a scale, and a screen that makes it possible to view small, sharply defined segments of the liquid at a time. The liquid to be tested is put into a cylinder with plane walls or a cell, and treated with enough indicator to give

a depth of color equal to that in the double wedge apparatus. The colors are matched against a white background.

The screen is moved until the color in the cylinder matches that in the field of vision of the wedge apparatus. If the scale

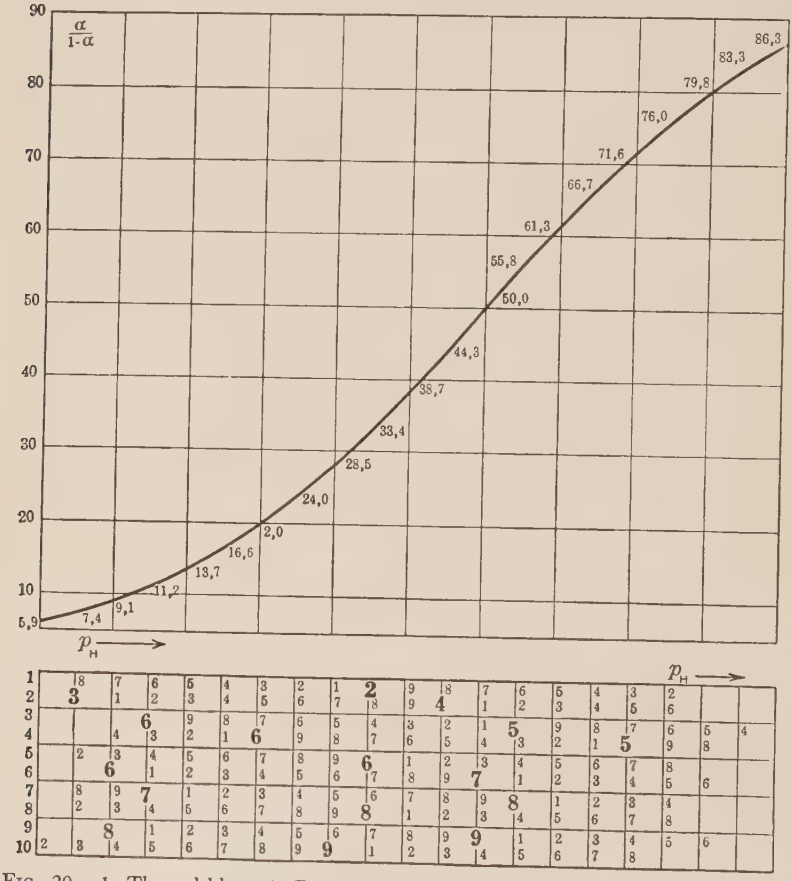

FIG. 20.—1. Thymol blue; 2. Brom phenol blue; 3. Methyl red; 4. Propyl red; 5. Brom cresol purple; 6. Brom thymol blue; 7. Phenol red; 8. Cresol red; 9. Thymol blue; 10. Cresol phthalein.

has been previously calibrated with buffer solutions of known hydrogen exponent, the p_H-value may be read off directly. This device is readily applicable to the determination of the p_H in the field in water investigations, since few other pieces of apparatus need to be used. It needs no long discussion to show that the

instrument may easily be used to advantage with other indicators, as methyl red, methyl orange, etc., for the rapid examination of physiological liquids, as urine, etc. The phthaleins can not be used because their alkaline solutions are unstable.

An improvement of the double-wedge method has been described by Kolthoff (21). Instead of standardizing the apparatus for one indicator it is so constructed that the ratio between the acid and alkaline form of an indicator may be read off. By using the equation:

$$[H^+] = K \frac{[HIn]}{[In^-]},$$

where K is the indicator constant, [HIn] the concentration of the acid form, $[In^-]$ that of the basic form, $[H^+]$ may be derived, or,

$$p_H = p_K + \log \frac{[In^-]}{[HIn]}.$$

It is necessary to know the value of p_K for the calculation. The following table contains the values determined by the author (21) using the double wedge, and also values determined by other investigators.

INDICATOR EXPONENTS FOR USE IN THE COLORIMETRIC DETERMINATION OF p_H WITHOUT BUFFER MIXTURES

Indicator	p_K According to			
	Kolthoff (21) 15°	Clark and Lubs (21)	Gillespie (21)	Holmesand Snyder (21)
Thymol blue (acid range)	1.62	1.70	1.70	1.52
Brom phenol blue	4.00	4.10	4.10	
Methyl orange	3.70			
Methyl red	4.05			
Brom cresol blue	5.10	.....	.....	4.68
Brom cresol purple	6.07	6.3	6.3	
Brom thymol blue	7.08	7.0	7.1	
Phenol red	7.85	7.92	7.7	
Cresol red	8.17	8.3	8.1	
Neutral red	6.85			
Thymol blue (alkaline range)	8.96	8.92	8.80	

L. Michaelis, A. Gyemant and R. Krüger (22) have developed a procedure for finding the hydrogen exponent with one-color indicators without the use of buffer mixtures. The basis is very simple. If we again consider an acidic indicator HIn that yields the colored anion In^-, we know that:

$$[H^+] = \frac{[HIn]}{[In^-]} K_{HIn}.$$

The In-ions determine the depth of color, C, of the solution. If the latter is known, we have $[HIn] = (1 - C)$, when a known quantity of indicator is added to the liquid. The derivation of p_H is made with the aid of the following equations:

$$p_H = p_{HIn} + \phi,$$

$$\phi = \log \frac{C}{1 - C}.$$

On page 204 of their communication these investigators give a table that shows the dependence of ϕ upon intensity of color, C.

THE FUNCTION ϕ OF COLOR INTENSITY, C (FROM MICHAELIS AND GYEMANT (22))

C	ϕ	C	ϕ	C	ϕ
0.002	−2.69	0.06	−1.20	0.35	−0.25
0.004	−2.40	0.08	−1.06	0.40	−0.18
0.006	−2.22	0.10	−0.95	0.50	0.00
0.008	−2.07	0.10	−0.95	0.50	0.00
0.010	−2.00	0.14	−0.79	0.60	0.20
0.01	−2.00	0.18	−0.65	0.70	0.38
0.015	−1.80	0.20	−0.59	0.80	0.60
0.025	−1.60	0.25	−0.47	0.85	0.75
0.04	−1.38				

The following indicators were used (see third chapter, pages 61 and 75):

(*a*) *β-Dinitro-phenol* 1, 2, 6; saturated aqueous solution. From the author's experience it seems better to use a 0.1 per cent solution in dilute alcohol (*cf.* Chapter III). Best range of use p_H 1.7–4.4 according to Michaelis; p_H 2.4–4 according to the author.

(*b*) *α-Dinitro-phenol* 1, 2, 4; saturated aqueous solution. The

author uses a 0.1 per cent dilute-alcoholic solution. Best range p_H 2.0 to 4.7 (Michaelis); 2.6 to 4.4 (Kolthoff).

(*c*) *γ-Dinitro-phenol* 1, 2, 5; saturated aqueous solution. Kolthoff uses 0.1 solution in dilute alcohol. His experience shows p_H 4.0–5.8 to be best in practice.

(*d*) *p-Nitro-phenol:* The author uses a 0.3 per cent aqueous solution. Michaelis found the p_H-range 4.7 to 7.9 to be best. The author found range 5.6–7.6 best.

(*e*) *m-Nitro-phenol:* The author uses 0.3 per cent aqueous solution, and recommends its use for p_H-range 6.6–8.6, while Michaelis finds 6.3 to 9.0.

(*f*) *Phenol phthalein:* Michaelis uses an 0.04 per cent solution in 30 per cent alcohol; the author a 0.1 solution in 50 per cent alcohol. Region of best application, p_H 8.5–10.5 (Michaelis); p_H 8.2–10.0 (Kolthoff).

(*g*) *m-Nitro-benzene-azo-salicylic Acid* (Salicyl yellow): The author uses two solutions; a 0.1 per cent solution in alcohol between p_H 10 and 11; a 0.025 per cent solution in 25 per cent alcohol between p_H 11 and 12.

The following considerations, about amount of indicator to be used, apply to the concentrations given by Michaelis and Gyemant.

A measured amount of the solution under examination, for example, 5 or 10 cc., is treated with enough of a suitable indicator solution, measured with a pipette, to give a very pale coloration. The amount of indicator solution may if necessary amount to 1 cc., but it is better in general to use only 0.5 or 0.1 cc. The amount used must be measured exactly.

An indicator that is adapted to the circumstances must be selected; when 0.2 to 1 cc. is used the color must be plainly visible but not too intense.

The author uses not more than 0.1 to 0.2 cc. of his solutions per 10 cc. of liquid.

In a second tube is placed from 4 to 9 cc. of about 0.01 N sodium hydroxide. For the indicators α-, β-, and γ-dinitrophenol conductivity water may be used equally well according to the author's experience. Enough of the same indicator is

now added to develop a color approximately equal to that in the first tube. As a rule a suitably diluted portion of the indicator stock-solution is used,—about a ten- or twenty-fold dilution; this is added from a burette graduated to 0.01 cc. divisions. It is then brought up to the same volume as that in the first tube (using 0.01 N alkali or water). The ratio between the amounts of indicator in the colored alkali and the solution under examination is equal to the color intensity, C (*cf.* table, page 160).

According to Michaelis the determination may be made much more simply by prepared series of indicator solutions that are stable for several months. The differences in p_H from tube to tube amount to 0.2 p_H. From the equation:

$$p_H = p_{HIn} + \log \frac{C}{1 - C}$$

it may be calculated simply for every indicator and every desired p_H how much of the fully alkaline form of the indicator must be placed in a comparison tube if a constant amount of indicator is always added to the solutions to be tested. The color comparison may be made advantageously in a comparator (Hurwitz, Meyer, and Ostenberg, *cf.* also page 169).

It should be observed that according to W. Windisch, W. Dietrich, and P. Kolbach (23), and the author's experience also, the alkaline comparison solutions are not stable. Therefore Windisch (loc. cit.) has suggested the use of potassium chromate, bichromate, or solutions of the two salts for comparison purposes.

The author (24) attempted to get along with two comparison solutions for the various indicators, using a chromate solution for α-dinitro-phenol and *p*-nitro-phenol, and a bichromate solution for γ-dinitro-phenol, *m*-nitro-phenol, and salicyl yellow. The details are given (*vida infra*).

The original direction of Michaelis is still the best, namely to prepare fresh indicator comparison solutions for the measurements. Naturally p_{HIn} must be known for the calculation of p_H from ϕ.

The value of p_{HIn} depends upon the salt content (see salt

error, page 179), and the temperature (page 182). The author used results of Michaelis and his co-workers to derive the values of p_{HIn} at a salt content of about 0.05 to 0.1 N at a temperature of about 15°; these are given together with temperature coefficients valid between 10° and 25°. The values derived by measurement (24) with buffer mixtures prepared according to Clark's directions, are also given.

p_{HIn} OF THE MICHAELIS INDICATORS AT 15° AND 0.05 N SALT CONCENTRATION

Indicator	p_{HIn} According to Michaelis	According to Kolthoff	Temperature Coefficient, Michaelis
β-Dinitro-phenol	3.62	3.58	0.006 $(15-t°)$
α-Dinitro-phenol	4.03	3.95	0.006 $(15-t°)$
γ-Dinitro-phenol	5.12	5.15	0.004 $(15-t°)$
p-Nitro-phenol	7.22	7.03	0.011 $(15-t°)$
m-Nitro-phenol	8.30	8.30	0.008 $(15-t°)$

Comparison with chromate or bichromate solutions which are stable for a year.

Flat-bottom tubes of colorless glass are used; aspirin tubes, for example, are very suitable. After filling with chromate or bichromate solution they are corked and numbered, and kept in a wooden box with blackened interior and small holes to hold the tubes. The base is white, either white-glass plate or paper. The color intensity of the solutions is judged by looking down toward the white background. In the determination of p_H the unknown solution is placed in a tube similar to that used for the reference solutions.

Ten cc. of the liquid are pipetted into the tube and the amount of indicator given in the table is added. The number of cubic centimeters of 0.1 per cent potassium chromate (Kahlbaum) or 0.1 per cent bichromate, that is placed in the comparison tube, is given in the table. It is then diluted to 10 cc.

The p_H can not be calculated simply from the color intensity, C, of phenol phthalein or salicyl yellow. Michaelis and Gye-

mant therefore give an empirical table for each of these indicators. The author (25) had previously determined the values, and found no exact agreement with the values of the aforementioned investigators. He was able to prove in other ways that his values were correct.

TABLE FOR 15°

Cc. 0.1% K_2CrO_4	0.3	0.45	0.7	1.1	1 5	1.8	2.3	3.1	3.7	4.0
That correspond to a p_H	2.95	3.18	3.35	3.55	3.75	3.95	4.15	4.35	4.60	
With α-dinitro-phenol (0.2 cc. 0.1% per 10 cc.).										
Corresponding to p_H of	(5.62)	5.70	5.78	5.93	6.1	6.24	6.45	6.8	7.05	7.15
With p-nitro-phenol as indicator (0.2 cc. 0.3% solution per 10 cc.).										
(0.1 cc. indicator per 10 cc.)	.....	.....	.....	.....	.....	7.13	7.36	7.55		

Temperature correction for α-dinitro-phenol 0.006 ($t-15$).
Temperature correction for p-nitro-phenol 0.011 ($15-t$).

CC. of 0.1% $K_2Cr_2O_7$	0.23	0.35	0.55	0 72	1.1	1.55	1 8	2 2	3.0
Corresponding to p_H of	3.95	4.05	4.25	4.45	4 65	4.85	5.05	5.25	5.45
With γ-dinitro-phenol (0.2 cc. of 0.1% per 10 cc.).									
Corresponding to p_H of	7.0	7.2	7.5	7.7	7.9	8.1	8.3	8.5	
Using m-nitro-phenol (0.4 cc. of 0.3% per 10 cc.).									
Corresponding to p_H of	.....	.....	.....	(9.8)	10.20	10.46	10.6	10.84	11.28
Using salicyl yellow (0.2 cc. of 0.05% indicator per 10 cc.).									
0.2 cc. of 0.025% indicator per 10 cc. p_H	.....	.....	10.2	10.4	10.8				

Temperature coefficient for γ-dinitro-phenol 0.004 ($t-15$).
Temperature coefficient for m-dinitro-phenol 0.008 ($t-15$).
Temperature coefficient for salicyl yellow 0.013 ($t-15$).

TABLE FOR PHENOL PHTHALEIN AT 18° (MICHAELIS)

C	p_H	C	p_H	C	p_H
0.01	8.45	0.21	9.20	0.65	10.0
0.030	8.60	0.34	9.40	0.75	10.2
0.069	8.80	0.45	9.60	0.845	10.4
0.120	9.00	0.55	9.80	0.873	10.5

VALUES FOUND BY KOLTHOFF (25)

C	p_H	C	p_H	C	p_H
0.0076	8.2	0.079	8.8	0.39	9.4
0.019	8.4	0.16	9.0	0.54	9.6
0.039	8.6	0.25	9.2	0.7	9.8

Temperature correction: 0.0110 $(t - 18°)$, according to Michaelis and Gyemant.

The following values hold for salicyl yellow at 20°.

TABLE FOR SALICYL YELLOW AT 20° (MICHAELIS)

C	p_H	C	p_H	C	p_H
0.13	10.00	0.36	10.80	0.75	11.60
0.16	10.20	0.46	11.00	0.83	11.80
0.22	10.40	0.56	11.20	0.88	12.00
0.29	10.60	0.66	11.40		

The author had worked out a similar procedure before the appearance of the work of Michaelis and Gyemant, and had extended it to the two-color indicators. As is known, every transition tint of one of the latter indicators corresponds to a definite p_H. If solutions are at hand that have the same shade as the indicator in its transition range, p_H may be determined easily with the aid of these solutions. Since most organic colored compounds are sensitive to light, mixtures of colored inorganic salts must be taken to preserve color comparison standards. Mixtures of ferric chloride and cobalt nitrate or chloride are very useful for neutral red, methyl orange, tropeolin 00, and the alkaline transition color of methyl red. Suitable solutions are: 11.262 g. $FeCl_36H_2O$ in 250 cc. of 1 per cent hydrochloric acid, or 18.2 g. crystalline cobalt nitrate in 250 cc. 1 per cent hydrochloric acid.

When neutral red, methyl red, and methyl orange are used

0.2 cc. of 0.05 per cent indicator solution is added to 10 cc. of liquid; for tropeolin 00 0.2 cc. of 0.1 per cent solution.

TABLE ACCORDING TO KOLTHOFF (25)

Ferric Chloride (Fe) = Cobalt nitrate (Co) = mixtures whose color corresponds to the p_H given.

Ratio Fe : Co	p_H			
	Neutral Red	Methyl Red	Methyl Orange	Tropeolin 00
0	....	5.19	3.05	1.98
0.1	6.98	....	3.22	
0.3	7.12	5.29	3.52	2.13
0.5	7.24	5.50	3.72	2.22
0.75	7.37	5.57	3.92	2.29
1.0	7.60	5.62	4.00	2.31
1.5	7.80	5.70	4.19	2.41
2.0	7.93	5.75	4.30	2.46
3.0	....	5.81	4.50	2.52

For comparison of color of methyl red in solutions of p_H smaller than 5.2 we may use mixtures of 0.004 N potassium permanganate and 0.01 N potassium bichromate in 0.4 N sulphuric acid. These comparison solutions are unstable, however.

For the determination of p_H in very small volumes of liquid by means of indicator papers see Chapter VII, page 226.

Recently W. R. Brode (26) made an excellent study of the use of a simple form of spectrophotometer for the determination of p_H without the use of buffer mixtures. As a matter of fact the experimental error with the spectrophotometric method is actually smaller than that in the usual visual method. W. C. Holmes (26) recommends the method and gives, in his preliminary paper, some details of the use of 1 naphthol 2 sodium sulphonate as an indicator (W. M. Clark, 1923). More recently F. Vles (26) has advised measurement at two different wavelengths to eliminate the error due to difference in concentrations

of indicator in the unknown and reference liquids. The ratio of the absorption coefficient at the two wave-lengths is:

$$\frac{(k_1c_1 + k_2c_2)}{(k'_1c_1 + k'_2c_2)}$$

where c_1 and c_2 are the concentrations of the acid or alkaline form of the indicator; k is the absorption coefficient. By applying the mass law expression we have:

$$[H^+] = K\frac{k_1 - k'_1}{k'_2 - k_2}.$$

This equation holds for cresol red and brom thymol blue, but not for crystal violet and methyl red. (This fact may be easily explained.)

5. Colored Solutions.—If the liquid under examination is colored the reference solution must be colored to about the same shade by a suitable indicator. Naturally only indicators that are not partly changed at the expected p_H may be used. If the liquid is, for example, yellowish brown with a $p_H = 7$, methyl orange may be used without hesitation to bring the reference solution to the same shade. Sörensen (2) has given a list of the most frequently used dyes:

(*a*) Bismarck brown 0.2 g. per liter of water.

(*b*) Helianthin 0.1 g. in 800 cc. of alcohol and 200 cc. of water; may be replaced by methyl orange 0.1 g. per liter of water.

(*c*) Tropeolin 0 0.2 g. per liter of water.

(*d*) Tropeolin 00 0.2 g. per liter of water.

(*e*) Curcumin 0.2 g. in 600 cc. 93 per cent alcohol and 400 cc. of water.

(*f*) Methyl violet 0.2 g. in a liter of water.

The following have proven to be quite useful:

(*g*) Methylene blue 0.1 g. per liter of water, and

(*h*) Safranine 0.1 g. per liter of water.

If the solution to be tested is turbid the comparison solution may be brought to the same turbidity, according to Sörensen, by

a suspension of barium sulphate freshly prepared by treating a small amount of 0.1 N barium chloride with an equivalent amount of potassium sulphate. A suspension of talc of kaolin will serve equally well if the material has been boiled with acid and washed with water, shaking frequently, until the washings no longer react acid to methyl red.

Henderson (27) dilutes strongly colored solutions until the color no longer interferes. Although the hydrogen-ion concentration of buffer mixtures is only slightly dependent on the total electrolyte concentration, the degree of dissociation is affected by great dilution. The procedure may therefore be recommended only when the desired accuracy is not too high.

Obviously colorimetric determinations of p_H in colored or turbid solutions are not very sharp. It is advantageous to use indicators in such determinations that are of different color from that of the solution. Thus, for example, phenol phthalein should be used with yellow solutions and not *p*-nitro phenol.

In many instances the artifice of extracting the colored material with ether, etc., may be used. The amount of the substance that can be extracted depends upon the partition coefficient and also upon the hydrogen-ion concentration, so that the color intensity of the ether layer may be compared with that of an ether extract prepared in an analogous way from the reference solution. Eosin iodide is a well-adapted indicator because its colored form is readily soluble in ether. Further investigation is needed to show whether it is possible to establish a complete series of indicators so that any p_H may be measured with sufficient accuracy by this procedure. It is obvious that the transition range of the indicator will be changed by the addition of the extraction agent.

Walpole (28) has devised a very excellent instrument for colored or very turbid solutions, that is explained in Fig. 21. *Cf.* also the apparatus of W. Biehler (29).

A B C D are short glass cylinders with plane bottoms that stand in cases of black paper over a brightly illuminated background. A contains 10 cc. of the solution to be tested, with added indicator. C contains 10 cc. of water. D contains 10 cc. of the solution to be tested, without the indicator. Finally B contains

10 cc. of the comparison solution, with indicator. The intrinsic color of the solution is thus canceled. Fig. 22 gives the arrangement of Clark and Lubs (5), and may be understood without further explanation.

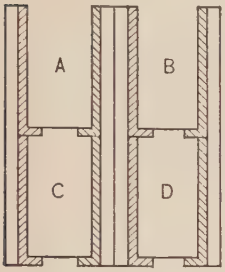

FIG. 21.

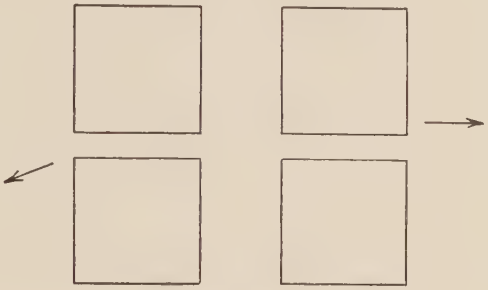

FIG. 22.

6. Sources of Error in Colorimetric Determinations.—(*a*) Solutions of very weak acids or bases, or small amounts of strong electrolytes. Friedenthal (30), Salm (31), and Sörensen (2) state that a solution must be tested for the presence of sufficient electrolytes before it is examined colorimetrically. According to them, the acid or basic character of the indicator plays a rôle in unbuffered solutions, and therefore affects the p_H-value. They state that the p_H of pure water or solutions of salts of strong acids or bases can not be determined in this way. The author does not agree entirely with this viewpoint. The deviation depends upon the indicator that is used. Assuming that in the examination of pure water an acid indicator, HIn, of dissociation constant 10^{-8} is used, we have:

$$HIn \rightleftarrows H^+ + In^-,$$

and if we take the following equation into account:

$$H_2O \rightleftarrows H^+ + OH^-,$$

we obtain the relation:

$$[In^-] = [H^+] - [OH^-],$$

since the liquid is electrically neutral. Then it follows from the expression for the dissociation constant of an acid that:

$$\frac{[H^+]\,([H^+] - [OH^-])}{[HIn]} = K_{HIn},$$

or

$$[H^+]^2 = K_{HIn} \times [HIn] + K_{H_2O}.$$

The concentration of indicator usually amounts to 5–10 drops of 0.1 per cent solution corresponding to a concentration of HIn = about 10^{-6} molar. Upon introducing this value in the above equation, we find:

$$[H^+]^2 = 10^{-8} \times 10^{-6} + 10^{-14} = 2 \times 10^{-14},$$
$$[H^+] = 1.4 \times 10^{-7}.$$

In this unfavorable case the value of $[H^+]$ is 1.4 times greater than that of water. The neutral indicators are usually ampholytes of dissociation constant smaller than 10^{-8}. Thus the deviation is much smaller than the figure given.

The case is very different when phenol phthalein is added to a very dilute alkali solution or much methyl orange is added to a very dilute solution of a strong acid because these indicators bind a relatively large amount of the $[OH^-]$ or $[H^+]$. The colorimetrically determined color does not agree with the hydrogen-ion concentration originally present; the value found is too small.

The following example shows very clearly that we may make a large error if we neglect the acid properties of phenol phthalein in dealing with very dilute alkali solutions.

For the sake of simplicity we shall assume that phenol phthalein acts as a monobasic acid of dissociation constant 10^{-9}. What will be the magnitude of the hydroxyl-ion concentration when 0.1 cc. 1 per cent phenol phthalein solution is added to 10 cc. of 0.0001 N sodium hydroxide? The indicator concentration, 100 mg. per liter, corresponds to approximately 3×10^{-4} molar concentration.

The indicator acid reacts with the alkali as follows:

$$HIn + OH^- \rightleftarrows In^- + H_2O.$$

It is therefore evident that the sum of the concentrations OH^- and In^- is equal to the total concentration of alkali at the start, or,

$$[OH^-] + [In^-] = 10^{-4}.$$

Since the total concentration of the indicator acid is 3×10^{-4}, the concentration of the undissociated part, HIn is:

$$[HIn] = 3 \times 10^{-4} - [In^-] = 3 \times 10^{-4} - 10^{-4} + [OH^-]$$
$$= 2 \times 10^{-4} + [OH^-].$$

Hence,

$$K_{HIn} = 10^{-9} = \frac{[H^+]\,[In^-]}{[HIn]} = \frac{K_{H_2O}\,(10^{-4} - [OH^-])}{[OH^-]\,(2 \times 10^{-4} + [OH^-])}.$$

Upon solving this equation we find $[OH^-] = 5 \times 10^{-6}$, while the original solution at the start had $[OH^-] = 10^{-4}$. The error is therefore very large.

Concerning the so-called "acid error" of *m*-nitro-phenol the reader is referred to the work of L. Michaelis and A. Krüger (22) and of Kolthoff (24).

F. W. Marsh (32) fears that indicator solutions may become alkaline upon storage in glass bottles for long periods. He gives directions for correcting for such error. The author has never found an error due to this cause, even in cases where the buffer capacity of the solution was very small.

7. Effect of Neutral Salts.—It follows from the investigations of Sörensen (2), Sörensen and Palitzsch (33), Bohdan von Szyskowski (34), and Kolthoff (35), that neutral salts may affect the color of an indicator, that of the acid indicators being shifted toward the alkaline side, and that of the basic indicators toward the acid side. Various theories have been advanced to explain the salt error, but none of them is adequate for the quantitative interpretation of the behavior of every indicator. The theories will not therefore be discussed here.

It should be borne in mind that neutral salts may also have an effect on the total acid or alkaline color of the indicator. Two different tendencies are operative to produce the salt error:

(1) The effect of the salt on the optical absorption by both forms of the indicator.

(2) Influence of salt upon the equilibrium relations of the two forms of the indicator.

The former effect is discussed in excellent papers by W. von Halben and L. Ebert (36).

The following observations of Sörensen (2) are introduced to give some conception as to the magnitude of the error; he investigated three solutions of 0.1 N hydrochloric acid. A was free from salts, B contained 0.1 N KCl and C 0.3 N KCl.

	p_H in		
	A	B	C
Calculated	2.02	2.04	2.06
Electrometric	2.01	2.01	2.05
Colorimetric with methyl violet	2.22	2.04	1.91
Colorimetric with mauvein	2.22	2.04	1.91
Colorimetric with methyl green	2.28	2.05	1.89
Colorimetric with methyl yellow extra	1.99	2.04	2.04

Sörensen and Palitzsch made comparative experiments by the calorimetric and electrometric methods in the determination of p_H in sea water. They found that the following corrections of the colorimetric values are necessary:

(*a*) *p*-Nitro-phenol: Reference solution,—phosphate mixture.

35 per cent salt	−0.12
20 per cent salt	−0.08

(*b*) Neutral red: Phosphate mixture as reference solution.

35 per cent salt	+0.10
20 per cent salt	+0.05

(*c*) α-Naphthol phthalein: Reference solution: phosphate mixture.

35 per cent salt	−0.16
20 per cent salt	−0.11

(*d*) Phenol phthalein: Reference solution: borax mixture.

35 per cent salt	—0.21
20 per cent salt	—0.16

The numbers are the necessary corrections. If, for example, the p_H of a solution containing 35 per cent of salt has been found to be 8.4, using phenol phthalein, the true value is 8.19. From the author's experiments it appears that the salt error is proportional to the concentration of salt. In general the error is negligible when the salt concentration is less than 0.2 N. It is only in case of very alkali-sensitive indicators like methyl violet, mauvein, methyl green, and certain sulphone phthaleins, that the correction must always be applied.

S. P. L. Sörensen and S. Palitzsch (37) later determined the salt error at very small salt contents. The correction in this case may be either positive or negative. *In judging the results, consideration must be given to the fact that probable salt errors are applicable in connection with the Sörensen buffer mixtures that were used in deriving the data.*

It was found that the salt error of neutral red was insignificant at salt concentrations smaller than 20 per cent, but this is not true for α-naphthol phthalein and phenol phthalein. The author has derived the following values from the graph of their results.

Salt Concentration, Per Cent	Correction for	
	α-naphthol phthalein	Phenol phthalein
0	+0.22	+0.22
2	+0.10 (phosphate buffer) +0.04 (borax buffer)	0.00
4	+0.06 (phosphate buffer) −0.02 (borax buffer)	−0.04
10	−0.03 (phosphate buffer) −0.09 (borax buffer)	−0.10
20	−0.17 (phosphate buffer) −0.10 (borax buffer)	−0.16

McClendon (38) determined the salt errors in mixtures of boric acid and borax with a total salt concentration of at most 0.6 N, for the indicators *o*-cresol sulphone phthalein and α-naphthol phthalein. When the salt concentration has risen to 0.5 N the value found must be corrected to the extent of −0.05; when the salt concentration is 0.6 N the correction is −0.10.

The author (39) found a large error at small salt concentrations in case phenol phthalein is used. On the contrary Brightman, Beachem, and Acree (40) observed that the color depended but little on the salt concentration if it was less than 0.05 N. Wells (41) studied the effect of salt on cresol phthalein; from his work it appears that the error may be considerable. The salt error of cresol red has been studied by Ramage and Miller (42). Their data agree quite well with those of Wells.

Salt Error of Cresol Red (Ramage and Miller)

Salinity in Parts per 1000	Salt Error
5.0	−0.11
10.0	−0.16
15.0	−0.22
25.0	−0.25

The author wishes to call attention to the fact that these values refer to ordinary buffer mixtures that contain 0.06 to 0.1 N salt. If this concentration is expressed as potassium chloride it corresponds to 7.4 parts per 1000. The salt error should be zero at this value since buffer mixtures are always used in the determination of p_H. This is not the case according to Ramage and Miller's data, and therefore the author uses his own values.

According to J. T. Saunders (43) phenol red, thymol blue, brom thymol blue, and brom cresol purple have the same salt error when the salt concentration is below 0.1 N. When ordinary buffer mixtures are used in the comparison the salt error at 0.6 N concentration is:

Salt Error (According to Saunders)

Indicator	Salt Concentration	Salt Error
Brom cresol purple	0.6 N	−0.25
Brom thymol blue	0.6 N	−0.19
Phenol red	0.6 N	−0.15
Cresol red	0.6 N	−0.18
Thymol blue	0.6 N	−0.18

These values are in good agreement with those of the author. The salt error of cresol red may be derived from the curve given in Fig. 23.

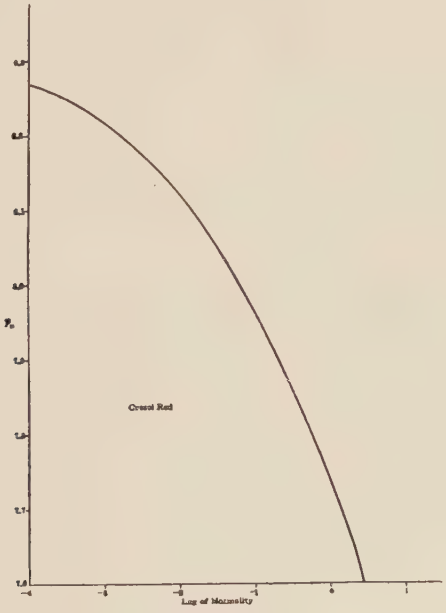

Fig. 23.

The author's experiments showed that in contrast with cresol red, the salt error of brom cresol phthalein is negligibly small. For thymol phthalein the error between p_H 8.0 and 9.8 is just as large as for phenol phthalein, while between p_H 1.2 and 2.8 it is very small.

On the contrary the salt error of tetra-brom phenol sulphone phthalein is very large at small salt concentrations. Very dilute precisely prepared hydrochloric acid solutions were compared with biphthalate-hydrochloric acid mixtures. 0.0004 N acid ($p_H = 3.4$) had the same color with the indicator as a buffer mixture whose p_H was 3.0–3.1; this corresponds to a hydrogen-ion concentration of about 0.001 N. If enough sodium chloride was added to bring the salt concentration to 0.05 N, the correct value 3.4 was found. When the salt concentration was 0.2 N the color corresponded to $p_H = 3.6$, and in presence of 0.5 N salt to a p_H of 3.8.

With acetic acid, results similar to those with hydrochloric were obtained. In using tetra-brom phenol sulphone phthalein one should be very careful to have the same concentration of salt in both reference and unknown solutions.

As may be seen from the next table, the salt errors of congo red, azolitmin, and tropeolin 0 are so large that these indicators should not be used in colorimetric determinations. In an exhaustive investigation the author has determined the salt errors of various hitherto unstudied instances. It should be noted that in study of the indicators between brom cresol purple and nitramin the p_H-values of the buffer solutions containing salt were determined with the hydrogen electrode. On the contrary, freshly prepared solutions of hydrochloric acid and salt were used for those between tropeolin 00 and brom cresol purple; the hydrogen exponent of the solutions was calculated, using the rule that the degree of dissociation of hydrochloric acid in salt mixtures is the same as that corresponding with the total electrolyte concentration. The salt errors of nitramin and tropeolin 0 were derived in the same way, using dilute sodium hydroxide.

It should be noted that Zoller and Harper (47) found that phthalate buffers give a violet precipitate with methyl violet between p_H 2.2 and 3.0. Proteins behave in the same manner.

Attention is called to the fact that phenol, for example, has a characteristic action on various indicators like methyl violet and methyl yellow.

SALT ERRORS OF INDICATORS (KOLTHOFF (44))

Indicator	Salt Added	Salt Concentration	Correction in p_H	Remarks
Tropeolin 00	KCl	0.1 N	−0.05	Very satisfactory indicator.
Tropeolin 00	KCl	0.25 N	−0.01	NaCl has the same effect as KCl.
Tropeolin 00	KCl	0.5 N	+0.06	
Tropeolin 00	KCl	1 N	+0.23	
Thymol blue (at the intermediate stage, p_H 1.2–2.8)	KCl	0.1 N	−0.06	Very suitable indicator.
Thymol blue (at the intermediate stage, p_H 1.2–2.8)	KCl	0.2 N	−0.06	NaCl same as KCl.
Thymol blue (at the intermediate stage, p_H 1.2–2.8)	KCl	0.5 N	−0.04	
Thymol blue (at the intermediate stage, p_H 1.2–2.8)	KCl	1.0 N	+0.05	
Methyl orange	KCl	0.1 N	−0.08	Very suitable indicator.
Methyl orange	KCl	0.25 N	−0.08	NaCl about the same as KCl.
Methyl orange	KCl	0.5 N	+0.02	
Methyl orange	KCl	1.0 N	+0.23	
Methyl yellow	KCl	0.1 N	−0.08	Similar to methyl orange, but not satisfactory because indicator rapidly separates at higher salt concentrations.
Brom phenol blue	KCl	0.1 N	−0.05	Larger error at smaller salt concentrations. Not suitable for investigation of very dilute solutions of electrolytes.
Brom phenol blue	KCl	0.25 N	−0.15	
Brom phenol blue	KCl	0.5 N	−0.35	
Brom phenol blue	KCl	1.0 N	−0.35	
Brom phenol blue	NaCl	0.1 N	−0.15	
Brom phenol blue	NaCl	0.5 N	−0.27	
Brom phenol blue	NaCl	1 N	−0.35	Richter (1925).
Congo red	NaCl	0.1 N	0.0	Unsatisfactory for colorimetric determination.
Congo red	NaCl	0.2 N	−0.25	
Congo red	NaCl	0.5 N	−0.55	
Congo red	NaCl	1.0 N	−0.9	
Brom cresol purple	NaCl	0.5 N	−0.25	Satisfactory indicator.
Methyl red	NaCl	0.5 N	+0.1	Very suitable indicator.
p-Nitro-phenol	NaCl	0.5 N	−0.05	Very suitable indicator.
Azolitmin	NaCl	0.5 N	−0.55	Unsatisfactory; large error at other salt concentrations.
Phenol red	NaCl	0.5 N	−0.15	The sign of the correction changes at very slight salt concentrations.
Neutral red	NaCl	0.6 N	+0.12	Saunders (1925).
Cresol red	NaCl	0.5 N	−0.20	
Brilliant yellow	NaCl	0.5 N	0.0	Suitable indicator.
Phenol phthalein	NaCl	0.5 N	−0.17	Suitable indicator.
Thymol blue (in transition range. p_H 8.0–9.6)	NaCl	0.5 N	−0.17	Suitable indicator.
Nitramin	KCl	0.1 N	−0.06	Suitable indicator.
Nitramin	KCl	0.25 N	−0.10	NaCl has about the same effect.
Nitramin	KCl	0.5 N	−0.10	
Nitramin	KCl	1.0 N	−0.16	
Tropeolin 0	KCl	0.1 N	+0.38	Not satisfactory.
Tropeolin 0	KCl	0.25 N	+0.44	
Tropeolin 0	KCl	0.5 N	+0.53	
Tropeolin 0	KCl	1 N	+0.62	

The salt error of nitramin has been determined by the author (45) for different salts with the following results:

SALT ERROR OF NITRAMIN

Salt Added	Concentration of Salt	Salt Error
KCl	0.5 N	−0.10
KCl	1.0 N	−0.16
KBr	0.5 N	−0.09
KBr	1.0 N	−0.12
$KBrO_3$	0.5 N	−0.08
$KBrO_3$	1.0 N	−0.17
NaCl	0.5 N	−0.07
NaCl	1.0 N	−0.08
Sodium Acetate	0.5 N	−0.09
Sodium Acetate	1.0 N	−0.22
K_2SO_4	0.5 N	−0.22
K_2SO_4	1.0 N	−0.30
Na_2SO_4	0.5 N	−0.13
Na_2SO_4	1.0 N	−0.27
Rochelle salt	0.5 N	−0.15
Rochelle salt	1.0 N	−0.19
Trisodium Citrate	0.5 N	−0.15
Trisodium Citrate	1.0 N	−0.20
$K_4Fe(CN)_6$	0.5 N ($\frac{1}{8}$ molar)	−0.20
$K_4Fe(CN)_6$	1.0 N ($\frac{1}{4}$ molar)	−0.34

The salt error is usually considered to be important at high salt concentrations and it would be natural to assume that the error is negligible at very low salt concentrations. That this is not the case, however, has been shown by the facts of the behavior of brom phenol blue in dilute hydrochloric acid in the presence or absence of a trace of salt (*cf.* page 174). The author (46) has therefore conducted a special investigation of salt error of indicators at very low salt concentrations. Buffer mixtures were diluted to various electrolyte contents; the p_H was determined by means of the hydrogen electrode and also colorimetrically by comparison with the Clark buffer mixtures. The salt errors are therefore related to the buffer mixtures.

SALT ERROR OF INDICATORS AT LOW ELECTROLYTE CONCENTRATIONS IN RELATION TO THE BUFFER MIXTURES OF CLARK (KOLTHOFF)

Total Electrolyte Concentration	Thym. Bl.	Ph. Pht.	Napth. Bl.	Ph. Red	Cr. Red	Neut. Red	Brom Th. Blue
0.001 N	+0.25	+0.25	+0.18	+0.35	+0.17	−0.09	+0.19
0.005 N	+0.19	+0.19	+0.14	+0.28	+0.15	−0.04	+0.17
0.01 N	+0.13	+0.14	+0.10	+0.22	+0.12	0.00	+0.15
0.02 N	+0.05	+0.06	+0.00	+0.15	+0.09	0.00	+0.12
0.03 N	.....	.....	.....	+0.09	+0.07	0.00	
	Chlor. Ph. Red	Brom Cr. Purple	Brom Cr. Blue	Methyl Red	Alizarine	Meth. Orange	Brom Ph. Blue
0.001 N	+0.47	+0.13	+0 45	+0.17	+0.25	−0.15	+0.25
0.005 N	+0.3	+0.10	+0.24	+0.10	+0.18	−0.07	+0.20
0.01 N	+0.21	+0.09	+0.16	+0.06	+0.12	−0.06	+0.17
0.02 N	+0.15	+0.08	+0.10	+0.03	+0.10	−0.04	+0.15
0.03 N	+0.09	+0.07	+0.07	0.00	+0.06	−0.02	

We see that α-naphthol blue, cresol red, neutral red, brom thymol blue, brom cresol purple, methyl red, and methyl orange have the smallest error at low electrolyte content. These indicators are therefore recommended for measurements in very dilute solutions of electrolytes.

Michaelis and Gyemant (22) and Michaelis and Krüger (22) give the following corrections for the indicators that they use.

SALT ERRORS OF MICHAELIS' INDICATORS

Indicator	0.5 N Salt	0.15 N Salt	0.1 N Salt	0.05 N Salt
α-Dinitro-phenol	−0.20	−0.10		
β-Dinitro-phenol	−0.30	−0.12		
γ-Dinitro-phenol	−0.13	−0.07		
p-Nitro-phenol	−0.05	±0.00		
m-Nitro-phenol	−0.16	−0.11	−0.10	−0.05
Phenol phthalein	−0.20	−0.08		

8. The Effect of Proteins and Their Decomposition Products.—Here also it was Sörensen (2) who first showed that these substances might render the colorimetric determination of p_H difficult or impossible. The reason is that the proteins because of their amphoteric character may combine with both acidic and basic substances. Most azo-dyes and also congo red are entirely useless in this case. Methyl violet and related compounds are only slightly affected by the compounds in question. The phthaleins yield good results if only the decomposition products are present; when undecomposed proteins are present they may not be used. Only one indicator, *p*-nitro-phenol, gives good service in all cases. As Sörensen (2) has already emphasized, the protein effect seems to be smaller the simpler the constitution of the indicator.

A few examples introduced from the work of Sörensen (2) follow: *a* is an invertase solution containing as buffer mixture 6 cc. of citrate and 4 cc. of sodium hydroxide. *b* is a slightly acidified glue solution (about 2 per cent), *c* dilute hydrochloric acid about 2 per cent solution of Witte peptone, and *d* a 2 per cent white of egg solution.

	p_H in			
	a	*b*	*c*	*d*
Electrometric	5.69	4.98	4.92	5.34
Colorimetric, with sod. alizarine sulphonate	5.85	5.97	5.75	5.61
Colorimetric with lacmoid	5.75			
Colorimetric with *p*-nitro-phenol	5.75	.....	.....	5.39

The protein error of methyl red is very small as Sven Palitzsch (48) has shown. This is evident from the following measurements on approx. 2 per cent natural egg-white in dilute hydrochloric acid:

p_H Electrometric	p_H Colorimetric	Δ Electrometric-colorimetric
4.99	4.75	+0.24
5.16	4.90	0.26
5.53	5.27	0.26
5.60	5.39	0.21
5.68	5.41	0.27
5.70	5.48	0.22

The protein error of methyl red is usually small in the following protein solutions:

Nature of Solution	p_H Electrometric	p_H Colorimetric	ΔElectrometric colorimetric
1 per cent casein in hydrochloric acid plus phosphate	5.66	5.58	+0.08
Hydrochloric acid solution of hydrolyzed serum plus phosphate	**4.73**	**5.83**	**−1.1**
Similar to above, with more HCl	**3.96**	**4.75**	**−0.79**
2 per cent acidified (HCl) casein solution partially decomposed by pepsin	5.57	5.48	+0.09
2 per cent Witte peptone in hydrochloric acid with 0.1 N NaCl	4.88	4.91	−0.03
Solution similar to the above	4.83	4.83	±0.00
2 per cent egg-white, partly decomposed by pepsin	5.63	5.58	+0.05
Similar solution	5.27	5.19	+0.08
Similar solution further decomposed	5.27	5.24	+0.03
2 per cent gelatine solution+prim. phosphate.	5.57	5.51	+0.06
Similar solution	5.17	5.17	0.00

By special experiments Sörensen showed that slow combination between indicators and proteins takes place. For example, after 40 cc. of 0.5 per cent egg-white and 10 cc. N hydrochloric acid had been mixed the color of tropeolin 00 gradually changed from red to yellow. It was proved by measurements with the hydrogen electrode that the hydrogen-ion concentration had not changed during this time. From the author's measurements with milk it was found that the protein error may be easily demonstrated as follows: If enough hydrochloric acid is added

to the milk to bring the p_H to about 2, drops of methyl yellow or orange that fall in are colored red for an instant. Upon mixing, the color becomes yellow.

From the foregoing account it is evident that the colorimetric method for the determination of [H+] generally gives good results in the absence of proteins and large amounts of neutral salts.

If the procedure is to be used in the investigation of solutions that contain substances whose effect on the color of the indicator has not been studied (e.g., colloids, many organic compounds), the results must be compared with those obtained electrometrically. The measurement of hydrogen-ion concentration with the aid of the hydrogen electrode is to be regarded as the primary procedure.

9. Temperature Effect.—The effect of temperature on the sensitivity of indicators has been extensively discussed in the third chapter (pages 85 ff). Hence we will include here only a table that gives the change in indicator exponents between 18 and 70°.

CHANGE OF INDICATOR EXPONENT BETWEEN 18° AND 70° (KOLTHOFF)

Indicator	Change Expressed in		Ratio of Dissociation Constant at at 70° to that at 18°
	p_H	p_{OH}	
Nitramin	−1.45	0.0	1
Phenol phthalein	−0.9 to −0.4	−0.55 to −1.05	About 5
Thymol blue	−0.4	−1.05	2.5
α-Napthol phthalein	−0.4	−1.05	2.5
Curcumin	−0.4	−1.05	2.5
Phenol red	−0.3	−1.15	2
Neutral red	−0.7	−0.75	
Brom cresol purple	0.0	−1.45	1
Azolitmin	0.0	−1.45	1
Methyl red	−0.2	−1.25	
Lacmoid	−0.4	−1.05	2.5
p-Nitro-phenol	−0.5	−0.95	3.2
Methyl orange	−0.3	−1.15	14
Methyl yellow	−0.18	−1.17	15
Brom phenol blue	0.0	−1.45	1
Tropeolin 00	−0.45	−1.0	10
Thymol blue	0.0	−1.45	1

Michaelis and his collaborators have determined the indicator exponents, p_{HIn}, of the indicators that they used, at various temperatures. Their results are collected in the following table:

p_{HIn} OF THE MICHAELIS INDICATORS AT VARIOUS TEMPERATURES

Temperature	α-Dinitrophenol	β-Dinitrophenol	γ-Dinitrophenol	*p*-Nitrophenol	*m*-Nitrophenol
5°	4.13	3.76	5.21	7.33	8.43
10°	4.11	3.74	5.18	7.27	8.39
15°	4.08	3.71	5.15	7.22	8.35
20°	4.05	3.68	5.14	7.16	8.31
30°	3.99	3.62	5.09	7.04	8.22
40°	3.93	3.56	5.04	6.93	8.15
50°	3.88	3.51	4.99	6.81	8.07

The temperature coefficient for phenol phthalein is 0.011 per degree, and the correction is subtracted at temperatures above 18°. For salicyl yellow the coefficient is 0.013, and the correction is subtracted at temperatures above 20°.

10. The Alcohol Error.—The effect of alcohol on the sensitivity of various indicators has been discussed in the third chapter (page 92 ff). The author has assembled the corrections, derived from experimental results, for the range 0 to 70 volume per cent of alcohol in the table that follows. The corrections apply at a temperature of 11–12°. Athough the temperature coefficient is quite large we may assume for alcohol contents up to 70 per cent that the values hold for temperatures between 10 and 20°. Because of the difficulties in determining the sensitivity ratio for the acid-sensitive indicators, phenol phthalein, thymol blue and thymol phthalein, the values given for them are quite uncertain.

The corrections are given in the same way as those for the salt error. A positive sign means that the correction given is to be added to the colorimetrically determined p_{H} to arrive at the correct p_{H}. If, for example, the correction for methyl orange in 50 per cent alcohol is −1.2, the 1.2 must be subtracted from the determined value to obtain the correct p_{H}. It should be noted that the neutral indicators that change between p_{H} 5 and 8

are not included in the table because we do not yet have buffer mixtures for the determination of the alcohol error.

ALCOHOL ERROR OF INDICATORS EXPRESSED IN p_H, AT 12°

Alcohol Content in Vol., Per Cent	T. B.	Tr. 00	B. P. B.	M. Y.	M. O.	Curc.	Phph.	T. B.	Thph.	Tr. 0	Nitr.
10	0.00	−0.06	0.06	−0.11	−0.10	−0.1	0.06	0.15	0.1	0.2	−0.25
20	0.02	−0.23	0.21	−0.24	−0.20	−0.3	0.10	0.3	0.3	0.25	−0.6
30	0.07	−0.6	0.35	−0.48	−0.47	−0.4	0.1	0.5	0.6	0.3	−0.9
40	0.15	−1.0	0.38	−0.8	−0.9	−0.5	0.45	0.7	1.0	0.5	−1.05
50	0.21	−1.4	0.38	−1.1	−1.2	−0.6	1.0	0.8	1.3	0.65	−1.1
60	0.25	−1.7	0.77	−1.4	−1.5	−0.5	1.6	0.9	1.6	0.8	−1.15
70	0.30	−1.9	1.0	−1.7	−1.8	−0.5	2.2	1.0	1.9	0.9	−1.25

T. B. = thymol blue; Tr. 00 = tropeolin 00; B. P. B. = brom phenol blue; M. Y. = methyl yellow; M. O. = methyl orange; Curc. = curcumin; Phph. = phenol phthalein; Thph = thymol phthalein; Tr. 0 = tropeolin 0; Nitr. = nitramin.

L. Michaelis and M. Mizutani (51) have extended the method of Michaelis and Gyemant, using nitro-indicators (*cf.* page 160), to alcoholic solutions. Liquids of well-known p_H were lacking for the determination of the dissociation of the nitro-indicators in alcoholic solution. They measured the p_H of such solutions against aqueous solutions of known p_H, using the electrometric method; they assumed that the alcoholic solution had the same p_H as the aqueous when the potential difference between hydrogen electrodes in the two solutions was zero. Hence they have used the assumption that the constant of the hydrogen electrode is the same in alcoholic as in aqueous solution, which probably does not hold exactly.

If the p_H of the alcoholic solution is known the changed indicator constant is found by the equation:

$$K' = a_H \frac{C}{1 - C},$$

a_H being the hydrogen-ion activity; C the color intensity. It is assumed that the ratio of the activities of indicator anion and undissociated acid remains unchanged under the different conditions.

Practical Directions for Measurement of p_H in Alcoholic Solutions.—The directions are broadly similar to those for aqueous solutions, with the difference that the alkaline reference solutions must have the same alcohol content as the solution under examination. The alkalinity necessary to develop the maximum color intensity is furnished by 0.01 N sodium hydroxide for alcohol percentages 0 to 70 and by 0.1 N alkali at higher alcohol content.

The calculation of p_H is made in the same manner as for aqueous solutions, using the p_K corresponding to the alcohol concentration. A special table is used for phenol phthalein.

The absolute accuracy of the method although not high is sufficient for approximate determinations.

TABLE OF p_K FOR NITRO-INDICATORS AT DIFFERENT ALCOHOL CONTENT (MICHAELIS AND MIZUTANI)

	p_K at Alcohol Content Expressed in Volume Per Cent of									
	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%
m-Nitro-phenol	8.37	8.56	8.75	8.97	9.15	9.40	9.64	9.92	10.24	10.73
p-Nitro-phenol	7.15	7.17	7.28	7.38	7.63	7.85	8.11	8.34	8.59	8.90
γ-Dinitro-phenol	5.15	5.20	5.23	5.39	5.45	5.58	5.70	5.95	6.08	9.40
α-Dinitro-phenol	4.00	4.00	4.00	4.00	4.00	4.15				

TABLE GIVING RELATION BETWEEN C AND p_H FOR PHENOL PHATHALEIN

C	p_H at an Alcohol Content, Expressed in Volume Per Cent of										
	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	95%
0.01	8.5	8.7	8.9	9.2	9.5	9.8	10.2	10.6	10.8	11.1	11.3
0.02	8.6	8.8	9.0	9.3	9.7	10.0	10.4	10.7	11.0	11.2	11.5
0.04	8.8	8.9	9.2	9.5	9.9	10.2	10.6	10.9	11.2	11.4	11.7
0.06	8.9	9.0	9.4	9.7	10.0	10.3	10.7	11.0	11.3	11.6	11.8
0.08	8.98	9.1	9.5	9.8	10.1	10.4	10.8	11.1	11.4	11.7	11.9
0.1	9.04	9.2	9.6	9.8	10.2	10.5	10.9	11.2	11.5	11.8	12.0
0.2	9.22	9.4	9.8	10.1	10.5	10.8	11.1	11.5	11.9	12.1	12.3
0.3	9.38	9.6	9.9	10.2	10.6	10.9	11.3	11.7	12.1	12.3	12.4
0.4	9.54	9.7	10.1	10.4	10.8	11.1	11.4	11.8	12.2	12.4	12.6
0.5	9.70	9.9	10.2	10.5	10.9	11.2	11.5	12.0	12.4	12.6	12.7

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CHAPTER VI

PRACTICAL APPLICATIONS OF THE COLORIMETRIC DETERMINATION HYDROGEN-ION CONCENTRATION

1. Water.—(*a*) *Distilled Water.*—(1) Distilled water is free from salts; if it were chemically pure $[H^+]$ would be equal to 8×10^{-8} at 18° ($[H^+] = \sqrt{K_{H_2O}}$). The reaction is always acid because of the presence of traces of carbon dioxide taken up from the atmosphere. Normal air contains about 0.3 per cent of carbon dioxide by volume; the partition ratio of carbon dioxide between gas phase and solution is about 1 : 1. Hence, water that has taken up carbon dioxide from the air until equilibrium is established, will also contain 0.3 per cent by volume, or about 0.0000135 mol. CO_2 concentration. Since the dissociation constant of carbonic acid is 3×10^{-7}, the solution has a $[H^+]$ of:

$$[H^+] = \sqrt{1.35 \times 10^{-5} \times 3 \times 10^{-7}} = 2 \times 10^{-6},$$

$$p_H = 5.70.$$

As a matter of fact it is found that the p_H of distilled water is usually about 5.7. The reaction of the water can not be determined with an ordinary methyl red solution (0.2 per cent in alcohol). As a result of a thorough investigation (unpublished) the author has arrived at the conclusion that such an indicator gives a strongly acid reaction (p_H about 5) to absolutely neutral water. The reason is that methyl red is itself an acid with a dissociation constant of 9×10^{-5}(15°). Hence 0.05 cc. of 0.2 per cent methyl red solution gives a p_H value of 4.7 to 5 cc. of neutral water. For many years the author determined the reaction of water with methyl red and of course always found it to be acid. To get good results, a neutralized methyl red solution must be used. 143 mg. of methyl red of high purity is dissolved

in 20 cc. of strong alcohol, 5 cc. of 0.1 N sodium hydroxide are added, and the volume is brought up to 100 cc. with water; 1 to 2 drops of indicator are added to 10 cc. of water. A p_H of 5.9 to 6.0 was found repeatedly for water in equilibrium with air. The calculated value is p_H 5.7; since the sodium salt of methyl red is used, a part of the indicator acid, HIn, is liberated with simultaneous transformation of carbonic acid to bicarbonate:

$$In^- + H_2CO_3 \rightleftarrows HIn + HCO_3^-.$$

The error that results is of no practical significance.

Neutral water, free from carbonic acid, has an alkaline reaction to the sodium salt of methyl red ($p_H = 6.2$). Such water may be obtained by boiling a high grade of distilled water (conductivity water) for one minute. It is not necessary to boil until less than two-thirds remain as L. E. Dawson (2) suggests. In the author's opinion it is dangerous to boil for so long a period (acids from flame; alkali from glass). After boiling, the vessel is closed with a one-hole stopper carrying a soda-lime tube.

Neutral water is very sensitive to traces of carbon dioxide from the air. Upon shaking for one minute with air the p_H becomes as low as 6.0. Neutralized brom thymol blue solution (made by Clark's directions) is most suitable for measuring the reaction of neutral water. The free indicator acid may not be used.

Dawson claims to have prepared water of p_H 7.0. The author never succeeded in obtaining such water; the values were always 6.6. to 6.7. It should be noted that in order to be sure that the indicator really gives the true p_H of the water special precautions must be taken as to the purity of the indicator and the preparation of its sodium salt. Dawson's finding of a p_H value of 7 may have been accidental. In any case it is necessary that neutral water should give a greenish color with neutralized brom thymol blue solution. The green color disappears if the solution is shaken for one minute in contact with air, the liquid remaining yellow. This last experiment gives a simple proof of the presence of alkaline impurities.

To summarize: The sodium salt of methyl red is needed for testing ordinary distilled water. If the p_H value found with this indicator is smaller than p_H 5.7 the water is too acid, too much carbonic acid usually being present. Such excess may usually be removed by passing pure air through. If the p_H value is still smaller than $p_H = 5.7$ the water has been contaminated by acids from the air. *Neutral water is alkaline to the sodium salt of methyl red*, and gives a green color with neutralized brom thymol blue solution.

It is evident, therefore, that the $[H^+]$ of distilled water may vary considerably. In contact with pure air the p_H will not be lower than 5.7. Ordinary distilled water is not pure enough for many purposes, e.g., for conductivity determinations. Water free from carbonic acid must be used; its conductivity should not be higher than about 1×10^{-6} at 18°. Such water is obtained by distilling water of higher conductivity over baryta (and if ammonia is present, the water is treated with Nessler's reagent). The water vapor is condensed in a metal condenser and carefully preserved. Such water should give the reaction mentioned in the preceding paragraph when tested with methyl red or brom thymol blue (neutralized solutions). Chemically pure water has been prepared only once, viz., by Kohlrausch and Heydweiller (3).

(*b*) *Drinking Water.*—The buffer system carbonic acid-bicarbonate is present in most drinking water. There are also varieties of water that give a plain alkaline reaction with phenol phthalein as they contain the system bicarbonate-carbonate. In this instance exact knowledge of the hydrogen-ion concentration has little significance. The case is different when free carbonic acid and bicarbonate are present. Various properties of water that are of practical importance are determined by the hydrogen-ion concentration and the absolute amount of carbonate and bicarbonate. For instance the action on lead pipes depends on these factors; also removal of iron, clarification of water, and removal of silicic acid (4). As soon as the hydrogen-ion concentration is known a preliminary decision with reference to the outstanding properties of the water may be

given, but only with certainty when the absolute amounts of carbonic acid and bicarbonate are known. The ability of water to attack calcium carbonate depends not only upon the hydrogen-ion concentration, but also upon the bicarbonate and calcium content. The table of Tillmans (5) that gives the hydrogen exponents, belonging to given bicarbonate concentrations, at which the water just fails to have corrosive action, may only be used when the number of equivalents of calcium equals that of the bicarbonate (*cf.* Kolthoff (5)). Aside from its value in judging water, knowledge of the hydrogen exponent is of great importance in analysis.

As has been repeatedly shown by various investigators, the determination of free carbonic acid, and especially of small amounts in the presence of bicarbonate, only yields good results when you use a constant amount of phenol phthalein, wait a sufficient length of time to see that the color is permanent, take care that no carbon dioxide escapes, and correct the value obtained in the titration for bicarbonate and calcium content. Furthermore, the carbonic acid content of the water is very apt to change whether by volatilization or by addition of alkali from the glass, so that it seems desirable to make the carbonic acid determination immediately upon taking the specimen from the well. In view of the well-known difficulties that are incumbent upon the carbonic acid titration, it is advantageous that it may be replaced by the simple determination of p_H.

From known bicarbonate and hydrogen-ion concentrations it may be deduced that

$$[CO_2] = \frac{[H^+]}{K_1} \times [HCO_3^-] = \frac{[H^+]}{3 \times 10^{-7}} \times [HCO_3^-].$$

By $[CO_2]$ we mean the total amount of carbonic acid, b, which is really $CO_2 + H_2CO_3$. Only a small portion of the carbon dioxide forms carbonic acid. The equation may only be used when the carbonic acid concentration is not less than $\frac{1}{10}$ of the bicarbonate concentration. If the carbonic acid concentration is small in comparison with the bicarbonate concentration the hydrolysis of the bicarbonate plays a rôle too important

to neglect. The total amount of carbonic acid is then greater than the free carbonic acid, b, that we determine by titration. Conversely, the total amount of bicarbonate is smaller than the quantity, a, that is found by titration. The author (5) has derived the values:

$$[CO_2] = b + a \times 1.2 \times 10^{-2},$$

$$[HCO_3^-] = 0.988a.$$

If these corrections are applied, almost the exact absolute amounts of $[CO_2]$ and $[HCO_3^-]$ that are present are found. The ordinary equation may then be used in the calculation:

$$[H^+] = \frac{[CO_2]}{[HCO_3^-]} \times 3 \times 10^{-7}.$$

Conversely, if these correction equations are taken into account it is possible to calculate the amount of carbonic acid knowing the values of $[H^+]$ and $[HCO_3^-]$. These corrections are practically independent of the absolution amounts of CO_2 and HCO_3^- and depend only on their ratio.

It is evident from the following table that large differences between the values for $[H^+]$ are found, when very small amounts of carbonic acid are present with relatively large amounts of bicarbonate, depending on whether the simple or exact equation is used in the calculation.

Ratio $\frac{\text{Carbonic acid}}{\text{Bicarbonate}}$	$[H^+]$ Calc. by Exact Equation	$[H^+]$ Calc. by Simple Equation
1 : 99	6.6×10^{-9}	3.0×10^{-9}
2.5 : 97.5	10.1×10^{-9}	7.5×10^{-9}
4 : 100	15.7×10^{-9}	12×10^{-9}
5 : 100	18.9×10^{-9}	15×10^{-9}
10 : 100	35×10^{-9}	30×10^{-9}

According to Wolman and Hannan (5) the hydrogen-ion concentration of water that is in equilibrium with the partial

pressure P of carbon dioxide and with calcite may be calculated by the equation:

$$[H^+] = K\sqrt{P[Ca^{++}]}.$$

K is a constant whose values depends upon the temperature.

J. T. Saunders (6) uses the formula of Prideaux to calculate the composition of mixtures of bicarbonate, carbonate, and carbonic acid from the experimentally determined p_H:

$$R = \frac{1 + 2\frac{K_2}{[H^+]} + \frac{K_W(K_1 + [H^+])}{[H^+]K_1C}}{1 + \frac{K_2}{[H^+]} + \frac{[H^+]}{K_1}}.$$

$K_1 = 3.04 \times 10^{-7}$; $K_2 = 6.0 \times 10^{-11}$; $K_W = 0.7 \times 10^{-14}$,

C = total concentration in equivalents per liter;

$$R = \frac{\text{equivalents of alkali}}{\text{moles } CO_2}.$$

When the water contains no free carbonic acid, i.e., when we have a mixture of carbonate and bicarbonate, the knowledge of the hydrogen exponent is without practical significance. The $[H^+]$ may be calculated if the concentration of carbonate and bicarbonate are known. The equation is not as simple as in the case of carbonic acid—bicarbonate (*cf.* Auerbach (7)). Since the determination of small amounts of carbonate in the presence of bicarbonate is not easy to make, it is better to calculate the carbonate concentration from the p_H and the bicarbonate concentration.

As has been said, most drinking water contains free carbonic acid and bicarbonate. For various reasons the determination of the hydrogen-ion concentration with the hydrogen electrode is not to be recommended in this case. It is only possible to obtain correct results by very careful work. A small amount of carbon dioxide is removed from the solution to the gas layer of the electrode, and the solution is very poor in buffers so that it must be shaken a long time during the determination. Also the salt content of the solution is usually small so that the electrical

resistance is high, thus rendering the potentiometric determination inaccurate.

Therefore it is only possible to obtain good results in solution containing carbonic acid by very careful work as Glenn E. Cullen and A. B. Hastings (8) have shown. The potentiometrically determined values agree exactly with the colorimetric.

The colorimetric procedure is therefore very well adapted to the determination of the p_H of drinking water. On the basis of various experiments the author has arrived at the conclusion that good results are obtained by the colorimetric and poor ones with the electrometric method. This fact is made clear in the following table. The experimental data are derived from the work of Massink (5). The calculated exponents were derived from the carbonic acid and bicarbonate content. As was to be expected the values determined by the hydrogen electrode are usually found to be too high because of loss of carbon dioxide.

	p_H Color.	p_H Elect.	p_H Calc.		p_H Color.	p_H Elect.	p_H Calc.
Almelo	7.2	.....	7.08	Meppel	6.2	6.86	6.15
Amsterdam W.	7.7	7.5	7.63	Nymegen	7.2	7.04	7.15
Apeldoorn	6.4	6.81	6.48	Oldenzaal	7.6	.....	7.62
Arnhem	6.0	6.59	6.2	Oosterbeck	7.4	.....	7.25
The Bosch	6.5	.....	6.6	Rhenen	7.35	7.46	7.34
Boskoop	7.6	.....	7.64	Sittard	7.4	.....	7.42
Breda	7.0	.....	6.96	Steenwijk	6.0	.....	6.09
Coevorden	6.8	.....	6.84	Tiel	.....	7.9	7.5
Eindhoven	7.5	.....	7.60	Utrecht	7.6	7.67	7.58
Enschede	7.2	.....	7.19	Valkenburg	7.6	.....	7.66
The Hague	7.6	7.87	7.80	Velp	7.0	.....	7.05
Heerlen C	7.0	6.87	7.05	Velsen	7.3	7.67	7.4
Heerlen K	7.5	7.39	7.55	Venlo	6.7	.....	6.76
Hoorn	7.3	7.52	7.38	Vlissingen	7.4	7.87	7.6
Leeuwarden	6.8	7.08	6.6	Voorburg	7.65	.....	7.63
Maarssen	7.9	8.04	7.8	Wageningen	6.9	7.3	6.74
Maastricht	7.5	7.58	7.45	Z. Beveland	7.7	7.87	7.75

The hydrogen exponent of most drinking water lies between p_H 7 and 8.0. Neutral red is the best indicator to use in the determination for various reasons. The transition interval is small, and the salt error is slight. Litmus, azolitmin, and rosolic

acid are not to be recommended. Phenol sulphone phthalein (phenol red) that also has a sharply defined transition interval is not suitable because of the rather large salt error at low concentrations of electrolyte. If p_H lies between 6.8 and 6.2 brom cresol purple may be used. If p_H is less 6.2 methyl red is appropriate. On the other hand, if p_H is between 8 and 9.5 phenol phthalein or thymol blue is satisfactory, and if p_H is even greater than 9.5 (which is seldom the case) thymol phthalein may be used. The reader is referred to the articles by Kolthoff (5) regarding other exceptional cases.

L. Michaelis (9) uses *m*-nitro-phenol without buffer mixtures in the determination of the p_H of sea water (see page 160). Since the indicator has a quite large acid error (*cf.* page 169) in solution that are poor in buffering power, the use of a small amount of indicator is recommended.

Michaelis gives the following directions: Use 25 cm. × 15 mm. (inner diameter) tubes with plane bottom; 40 cc. of water gives a depth of 22–23 cm. In a tube of this sort place 40 cc. of 0.01–0.02 N sodium hydroxide and 0.30 cc. of 1 : 3000 solution of *m*-nitro-phenol. 40 cc. of the water under examination should about match the color shade of this tube. The color is very pale, but the eye is most sensitive for fine differences in color tint under these conditions. The observations are made by daylight with a white porcelain background. According to the author's experience the accuracy of the procedure is not higher than 0.2 p_H for waters of p_H around 7.

(*c*) *Sea Water.*—As Sörensen and Palitzsch, who have carried out extended investigations of sea water, remark, the determination of the hydrogen exponent is best made in practice by the colorimetric method. The value for surface water lay between 7.95 and 8.35; only one exception was found, the water from the Black Sea, for which the exponent was 7.26. The higher hydrogen-ion concentration is to be ascribed to the presence of hydrogen sulphide. The p_H of water under the surface was usually between 8.07 and 8.09. W. E. Ringer (11) found the p_H of water from the North Sea and Zuyder Zee to be between 8.24 and 7.85. In connection with their investigations S. P. L.

Sörensen and S. Palitzsch (10) determined the salt errors of the indicators used.

Indicator	Buffer Mixture	Grams Salt per 1000 cc., Salt Error			
		35	20	5	1
p-Nitro-phenol	Phosphate	+0.12	+0.08		
Neutral red	Phosphate	−0.10	−0.05		
α-Naphthol phthalein	Phosphate	+0.16	+0.11	−0.04	−0.13
α-Naphthol phthalein	Borate	+0.22	+0.17	+0.03	−0.07
Phenol phthalein	Borate	+0.21	+0.16	+0.05	−0.03

A positive sign means that the colorimetrically found values are too high. If, for example, a p_H of 8.51 were found for a solution that contained 3.5 per cent salt using phenol phthalein, the true value would be 8.3.

With regard to the effect of the growth of algae on p_H of water the reader is referred to the work of R. Legendre (12), and V. Ulehla (12).

(*d*) *Mineral Waters.*—Mineral waters may react acid because of excess of carbonic acid or alkaline by reason of presence of the carbonic acid—bicarbonate combination. The p_H seems to be important in connection with their medicinal action. J. König (13) makes the following observations: "Recently the medical profession has laid much stress on the determination of the hydrogen-ion concentration of mineral water. Naturally it is not a question of the values determined by acidimetric or alkalimetric titration, but rather of the hydrogen-ion content. . . . We are now at the entrance of a recently disclosed but extremely promising realm, and at first chemists need only rarely to conduct exhaustive investigations."

The hydroxyl-ion concentration of alkaline mineral waters may be calculated from the bicarbonate and carbonate content, as has been done by Hintz and Greenhut (14) and Auerbach (15). Auerbach showed that the calculation according to Hintz and Greenhut was not entirely correct, and he gives improved equations. Thus Auerbach found for water from Kainz spring at $t = 8° : [OH^-] = 4 \times 10^{-4}$; from the Antonian spring at

26.7° : $[OH^-] = 6.3 \times 10^{-5}$; Sidonian spring at 9.5° : $[OH^-] = 2.58 \times 10^{-4}$. Michaelis (16) found electrometrically:

Mühlbrunnen	$p_H = 7.00$
Sprudel	$p_H = 6.80$
Marktbrunnen	$p_H = 6.54$

Considering the high carbonic acid content of these waters, the colorimetric method should also give a very good determination of the p_H.

Sewage.—The hydrogen exponent is also of significance in the purification of sewage. Sewage is freed from sludge by filtration; the speed of filtration depends not only on temperature but also on the p_H. Thus Wilson, Copeland, and Heisig (17) found that the speed of filtration of a sludge was greatest at a $p_H = 3$. The speed falls off if the reaction is more or less acid.

An interesting investigation by Olaf Arrhenius (18) has a bearing on the above findings; he studied the rate of settling of various clay suspensions at different p_H values. The particles were peptized in strongly acid or alkaline solution and then settled slowly. They settled most rapidly at $p_H = 4.7$, corresponding to the isoelectric point. If more acid is added the speed diminishes rapidly until $p_H = 4.0$ is reached; at stronger acid reaction the speed increases. When the p_H becomes greater than 4.7 the speed of settling again decreases to a marked extent, and between p_H 7.5–9 he obtained a stable emulsion that only broke up at higher alkalinity. In the opinion of the author the presence of polyvalent cations has a greater effect here than the hydrogen-ion concentration.

The hydrogen exponent plays an important rôle in the purification of turbid water with alum, as the investigation of W. D. Hatfield (19), for example, has shown. The best flocculation occurs between $p_H = 6.6$ and 7.6. This result is in agreement with that of Eddy (19) who found a maximum in the flocculation at $p_H = 7$.

2. Determination of the Dissociation Constants of Acids and Bases, and Testing of Acids for Acid or Basic Impurities.—(*a*) *Monobasic Acids and the First Dissociation Constants of Polybasic Acids.*—If the hydrogen-ion concentration of a solution

of known strength is determined, the dissociation constant may be calculated simply. The equation:

$$K_{HA} = \frac{[H^+]^2}{c - [H^+]},$$

always applies; c is the total concentration of the acid.

Salm (20) determined the constants of various acids by means of colorimetric determination of the hydrogen-ion concentration of solutions of known strength. Conversely, it is possible to identify an acid whose dissociation constant is known by measuring the $[H^+]$ of a solution of known strength. The author (21) calculated the $[H^+]$ of 0.1 N solutions of different acids, and also determined the value colorimetrically; the agreement was excellent. The various data are given for some acids that are of practical importance, in the following table. For phosphoric acid a 0.1 N solution is considered the same as an 0.1 molar. It may be seen directly from the table in Chapter V, page 137, what buffer mixtures are to be used as reference solutions. Freshly prepared hydrochloric acid solutions may be made of p_H values that agree with those of most of the acids that are to be examined.

TABLE OF $[H^+]$ OF VARIOUS ACIDS

Nature of Acid	Dissociation Constant	Strength of Solution	p_H	$[H^+]$	Indicator
Arsenious	6×10^{-10}	Saturated	5.0	1×10^{-5}	Methyl red
Boric	6.6×10^{-10}	0.1 N	4.84	1.45×10^{-5}	Methyl red
Phosphoric	1.1×10^{-2}	0.1 mol.	1.52	3.05×10^{-2}	Meth. violet or Trop. 00
Acetic	1.86×10^{-5}	0.1 N	2.86	1.4×10^{-3}	Trop. 00 or Thymol blue
Succinic	6.8×10^{-5}	0.1 N	2.75	1.8×10^{-3}	Trop. 00 or Thymol blue
Citric	8.2×10^{-4}	0.1 N	2.31	4.9×10^{-3}	Trop. 00 or Thymol blue
Hydrocyanic	7.2×10^{-10}	0.1 N	5.07	8.5×10^{-6}	Methyl red
Lactic	1.4×10^{-4}	0.1 N	2.43	3.7×10^{-3}	Trop. 00 or Thymol blue
Formic	2.05×10^{-4}	0.1 N	2.33	4.6×10^{-3}	Trop. 00 or Thymol blue
Oxalic	3.8×10^{-2}	0.1 N	1.56	2.75×10^{-2}	Meth. violet or Trop. 00
Tartaric	9.7×10^{-4}	0.1 N	2.19	6.5×10^{-3}	Thym. blue or Trop. 00
Benzoic	6.52×10^{-5}	0.01 N	3.10	8×10^{-4}	Trop. 00 or Thym. blue
Camphoric	2.29×10^{-5}	0.01 N	3.32	4.8×10^{-4}	Methyl orange
Saccharin (*o*-sulpho benzamide)	2.5×10^{-2}	0.01 N	2.13	7.5×10^{-3}	Trop. 00 or Thym. blue
Salicylic	1.06×10^{-3}	0.01 N	2.55	2.8×10^{-3}	Trop. 00 or Thym. blue
Veronal	3.7×10^{-8}	0.01 N	4.7	1.9×10^{-5}	Methyl red

The colorimetric determination may also be used to test the purity of acids. It is best for this purpose not to use an 0.1 N solution, but a more concentrated one. It is not possible to detect small amounts of mineral acids or of alkalies in all acids with great sensitivity. The smaller the dissociation constant the greater the change in $[H^+]$ for a small addition of strong acid or alkali. It was found that even in unfavorable circumstances 1 per cent of acid or alkali could be easily detected. A 0.2 molar solution of tartaric acid was made. Known amounts of hydrochloric acid or alkali were added and the $[H^+]$ determined colorimetrically with tropeolin 00 as indicator (thymol blue may also be used). The $[H^+]$ was also calculated.

It follows from the dissociation constant of tartaric acid that the $[H^+]$ of a 0.2 mol. solution is 1.4×10^{-2}. On adding enough hydrochloric acid to correspond to 0.01 N hydrochloric acid the $[H^+]$ is not equal to 2.4×10^{-2}, but is smaller because on addition of the stronger acid the dissociation of the tartaric acid is repressed. If the concentration of the dissociated acid is called x, and if a is the concentration of mineral acid or alkali, it may be derived from the equation involving the dissociation constant that:

$$\frac{(a + x)x}{0.2} = K = 9.7 \times 10^{-4}.$$

From this quadratic equation we may calculate x and hence $[H^+]$. Hence we find:

Composition of Solution	$[H^+]$ Found	$[H^+]$ Calc.
I. 0.2 mol. tartaric acid	1.4×10^{-2}	1.36×10^{-2}
II. Like I plus 2 equiv. per cent of HCl	1.7×10^{-2}	1.6×10^{-2}
III. Like I plus 2 equiv. per cent of NaOH	1.1×10^{-2}	1.2×10^{-2}
IV. Like I plus 4 equiv. per cent of NaOH	0.9×10^{-2}	1.0×10^{-2}

The smallest amount of acid or alkali added to an acid of smaller dissociation constant may be detected with still greater delicacy.

(*b*) *Very Weak Acids or Bases.*—The $[H^+]$ of concentrated solutions of weak acids is small; conversely the $[OH^-]$ in relatively concentrated solutions of weak bases is also small. If the

dissociation constant of such an acid or base is to be calculated from the colorimetrically determined $[H^+]$, traces of carbonic acid in the water, or traces of acidic or basic impurities in the substances to be studied exert such a large influence on the $[H^+]$ that the value for the dissociation constant will be erroneous. It is therefore better to use another method in such cases. If alkali is added to the solution of a very weak acid of dissociation constant equal to or greater than 10^{-10} the system acts as a buffer mixture, like that of a stronger acid. In the present instance practically all of the acid is converted into salt by the alkali, in any event when the original mixture is not too unfavorable, i.e., ratio acid: salt equal to or less than $\frac{1}{10}$; otherwise the hydrolysis of the salt must be considered in the calculation. If the acid under examination is half neutralized with alkali,

$$K_{HA} = [H^+] \times \alpha.$$

α is the degree of dissociation of the salt formed; this must be approximated in most cases. If only a tenth of the acid is neutralized, $K = \frac{1}{10}\alpha[H^+]$.

The dissociation constants of very weak bases may be determined in similar manner. It should be noted that the dissociation constants of stronger acids and bases may be determined in the same way.

The author (22) found the following values while testing the procedure:

Substance	Dissociation Constant
Phenol	9.2×10^{-11}
Resorcin	$K_1=3.0\times10^{-10}$; $K_2=8.7\times10^{-11}$
Aniline	1.9×10^{-10}
Semicarbazide	2.9×10^{-11}
Glycocoll	$K_a=1.2\times10^{-10}$; $K_b=2.3\times10^{-4}$

The dissociation constants of the alkaloids that were determined by the author will be found in Table III at the end of the volume.

The dissociation constants of exceedingly weak acids like cane sugar, etc., may be determined colorimetrically by using concentrated solutions and taking the hydrolysis into account.

(*c*) *Dissociation Constants of Polybasic Acids.*—The first dissociation constants may be determined in the same way as those of monobasic acids. The other constants must be derived in a different fashion. This may be done in two ways: one is by measurement of $[H^+]$ of mixtures of acid salt and the next salt (i.e., for dibasic acids the acid salt and the normal salt); the other consists in determination of $[H^+]$ of the solution of the acid salt. The former is simpler. From the equation:

$$HA^- \rightleftarrows H^+ + A^=,$$

it follows that

$$K_2 = [H^+]\frac{[A^=]}{[HA^-]}.$$

The $[H^+]$ may be determined in the way described under (*b*) and the constant calculated.

The constant may be calculated in about the same manner from the $[H^+]$ of the acid salt, according to Noyes (23). The constants may be derived as exactly and much more simply than those in the literature, in these two ways. The author found average values at 15° for the following acids:

SECOND DISSOCIATION CONSTANTS OF POLYBASIC ACIDS.

Oxalic acid	$K_2 = 3.5 \times 10^{-5}$
Succinic acid	$K_2 = 5.9 \times 10^{-6}$
Tartaric acid	$K_2 = 8. \times 10^{-5}$
Citric acid	$K_2 = 4.8 \times 10^{-5}$
Citric acid	$K_2 = 1.8 \times 10^{-6}$
Malic acid	$K_2 = 9. \times 10^{-6}$
Malonic acid	$K_2 = 3. \times 10^{-7}$
Maleic acid	$K_2 = 8. \times 10^{-7}$
Fumaric acid	$K_2 = 5. \times 10^{-5}$
Aconitic acid	$K_2 = 1.1 \times 10^{-6}$
Adipic acid	$K_2 = 5. \times 10^{-6}$
Mucic acid	$K_2 = 6.4 \times 10^{-5}$
Phthalic acid	$K_2 = 8. \times 10^{-6}$
Camphoric acid	$K_2 = 2.5 \times 10^{-6}$

3. Hydrolysis Constants.—We have seen (Chapter I, pages 14 ff) that the hydrolysis constant may be calculated simply, from the $[H^+]$ of a salt solution. Of the many methods that are

described in the literature (24) for the calculation of hydrolysis constants the colorimetric is perhaps the most suited. The inversion and hydrolysis methods must usually be carried out at elevated temperatures because of the small $[H^+]$ or $[OH^-]$ of the solution; the hydrolysis must be considerable if the electrical conductance method is to be applied. The hydrogen electrode is not applicable in many instances because of the presence of metals that stand below hydrogen in the potential series, and in case of many organic compounds because of reduction at the electrode; finally the partition method is of limited application. The colorimetric method may be used successfully in almost all cases except that of colored salts. It is often possible to place below the vessel containing the colored solution another cell (Fig. 21, page 169) containing a solution of color complementary to that of the upper solution. Thus the interfering color of cobalt salts may be removed by the use of a nickel salt in the lower vessel for $[H^+]$ measurement. The colorimetric method has been used in preference to others for organic compounds by Veley (24), Tizard (24), Barratt (24) for cinchona alkaloids; Denham (24) studied individual metal salts with the hydrogen electrode.

4. Examination of Salts for Basic or Acidic Impurities.— Salts of strong acids and bases in aqueous solution react exactly neutral, i.e., they do not change the reaction of water. As we have seen under § 1, the reaction of distilled water may vary considerably. Ordinarily it is only possible to use water saturated with air in the investigation of the salts, and it is then required that the salt shall not change the reaction that the water gives toward methyl red. This reaction is very sharp and excludes the presence of the slightest traces of acid or alkali. Practically it is better to require 10 cc. of 1 : 10 solution of the salt to react alkaline to phenol phthalein on addition of 1 drop of 0.1 N alkali, and acid toward methyl orange on addition of a drop of 0.1 N acid. Salts of weak acids react alkaline because of hydrolysis and those of weak bases with strong acids react acid. If the hydrolysis constant is known the $[H^+]$ of a solution of given concentration may be calculated. A colorimetric deter-

mination will prove whether the salt is entirely pure. These reactions should only be used in testing especially pure preparations; in testing of salts such as those used by druggists it is better to establish limits for the amounts of acid or alkali permissible. The following specifications may be established for commercial salts:

Potassium Acetate.—10 cc. of 1 : 10 solution treated with phenol phthalein gives the indicator a transition tint that is decolorized by 0.1 cc. of 0.1 N HCl. The presence of more than 0.1 per cent of carbonate is thus excluded.

Alkali Carbonate.—A 1 : 5 (for potassium carbonate 0.5 : 5) solution treated while hot with 20 cc. 0.5 N barium chloride and 3 drops of phenol phthalein should be colorless on cooling and should be colored permanently red by 0.1 cc. of 0.1 NaOH. An amount of one part in 2500 of free base or 1 in 1000 of bicarbonate may be detected in this way. If the barium carbonate is added at room temperature to the carbonate solution, pure carbonate reacts alkaline because a little barium bicarbonate is carried down with the carbonate (Sörensen, 1904).

Alkali Bicarbonate (25).—The German pharmacopeia sets a limit on the amount of acid that shall be required to decolorize a bicarbonate solution to which phenol phthalein has been added. Since the color change is not sharp it is not possible to judge accurately whether the preparation contains carbonate. The examination may be made better by adding just as much phenol phthalein to the solution as would barely fail to color a pure bicarbonate solution rose. If 0.2 cc. 1 per cent phenol phthalein is added to 50 cc. of pure 0.1 N bicarbonate in a Nessler cylinder the liquid is colorless, but becomes rose colored in presence of carbonate. The carbonate content may be derived from the intensity of the color. One per cent of carbonate may be thus detected in bicarbonate.

Sodium Phosphate.—A 1 : 10 solution treated with 3 g. of sodium chloride should react so feebly alkaline to phenol phthalein that the color is discharged on addition of 0.1 cc. of 0.1 N hydrochloric acid. One part per 1000 of carbonate may be detected in this way.

Sodium Phosphate—A 1 : 10 solution treated with 3 g. of sodium chloride should react so feebly alkaline to phenol phthalein that the color is discharged on addition of 0.1 cc. of 0.1 N hydrochloric acid. One part per 1000 of carbonate may be detected in this way.

Sodium Arsenate.—Should satisfy the same requirements as sodium phosphate.

Sodium Pyrophosphate.—A 1 : 20 solution saturated with sodium chloride should react so feebly alkaline to phenol phthalein that the color is discharged upon addition of 0.2 cc. 0.1 N HCl. This excludes the presence of 1 part per 1000 of carbonate.

Sodium Potassium Tartrate.—The 1 : 10 solution is colorless or so feebly alkaline toward phenol phthalein that the color is discharged upon addition of 0.1 cc. of 0.1 N HCl.

Potassium Antimonyl Tartrate.—The presence of potassium bitartrate may be very plainly shown with methyl orange or methyl yellow. A 1 : 20 solution of a pure preparation has a p_H of 4.1; upon addition of 1 per cent of bitartrate it becomes 3.4. Hence it is required that a 1 : 20 solution of the preparation under test shall not react more acid than an 0.1 mol potassium biphthalate solution. The presence of more than 0.3 per cent potassium bitartrate is thus excluded.

Sodium Salicylate.—The 1 : 10 solution should react acid to phenol phthalein and should become alkaline upon addition of 0.1 cc. of 0.1 N alkali.

Sodium Glyceryl Phosphate.—The 1 : 20 solution reacts feebly alkaline to phenol phthalein and is decolorized by 0.1 cc. 0.1 N HCl.

Sodium Phenol Sulphonate.—The 1 : 10 solution reacts alkaline to methyl yellow, and the solution becomes acid upon addition of 0.1 cc. 0.1 N HCl.

Zinc Chloride.—1 : 10 solution alkaline to methyl yellow and becomes acid on adding 0.1 cc. 0.1 N HCl.

Zinc Sulphate.—The presence of traces of acid must be avoided because the preparation is used in eye treatment. The 1 : 10 solution must react alkaline to methyl orange. The solution will then contain less than 1 : 200,000 of sulphuric acid.

Zinc Phenol Sulphonate.—10 cc. of 1 : 10 solution should react alkaline to methyl yellow and become acid to the indicator on addition of 0.1 cc. of 0.1 N acid.

Copper Sulphate.—The direct colorimetric determination of the reaction of the salt is difficult because of the blue color of the solution. Sodium thiosulphate may be used to convert the copper into the colorless cuprous ion. 20 cc. of N sodium thiosulphate are added to 10 cc. of the 1 : 10 solution, and the reaction toward methyl yellow is observed. It should be alkaline. The presence of 1 : 2000 of free sulphuric acid is then ruled out.

Ferrous Sulphate.—The 1 : 10 solution reacts alkaline to methyl yellow.

Ferric Chloride.—The 1 : 10 solution upon treatment with 10 mg. of copper sulphate and 6 cc. of N sodium thiosulphate should not separate out a brown turbidity on standing for three minutes, and should not require more than 0.2 cc. of 0.1 N alkali to turn methyl yellow.

Aluminium Sulphate and Alum.—The 1 : 20 solution of these preparations must react alkaline to tropeolin 00. This excludes the presence of more than 1 : 1000 of sulphuric acid.

The investigation of salts of weak acids and weak bases can not be made in the manner described because the solutions are more or less strongly hydrolyzed. It is best to treat the solutions with methyl red and determine the $[H^+]$. As we have seen in the first chapter (page 16), we may calculate the $[H^+]$ of solutions of salts of weak acids and bases. A solution of pure ammonium acetate gives an entirely neutral reaction. If the p_H at room temperature deviates from 7.1 we may calculate from the $[H^+]$ how much free acid or ammonia the preparation contains. The same considerations apply to ammonium oxalate; the solution of a pure preparation has a p_H of 6.88; of ammonium formate, 6.45; ammonium succinate, 7.3. Ammonium salicylate is easier to test. 50 cc. of the 1 : 50 solution should impart a transition tint to methyl red, and not more than 0.2 cc. 0.1 N alkali should be required to give the alkaline color. The testing of lead acetate for basic salt is more burdensome because such impurity only changes the reaction ($p_H = 6.0$) of lead acetate

slightly. The test must therefore be made differently: 10 cc. of 10 per cent sodium thiosulphate solution and then 15 cc. 0.5 N barium nitrate and 5 drops of phenol phthalein are added to 10 cc. of the 1 : 20 solution. The solution obtained must not react alkaline, but must give a permanent red color with 0.2 cc. of 0.1 N alkali.

5. Maximum Stability of Esters of Carboxylic Acids.—As is well known esters are saponified either in acid or alkaline solution. Hence they must have a minimum saponification rate or maximum stability at some definite p_H. Thus K. G. Karlson (26) found that methyl acetate has a maximum stability at p_H 4.70 at 88.5°, and ethyl acetate at $p_H = 5.1$. The reader is referred to work of H. v. Euler and Svanberg (26) concerning the theoretical significance of this point.

6. Minimum Solubility of Ampholytes.—These compounds as we have seen in the second chapter (page 41) may behave either as acids or bases. If both the salt with the acidic and that with the basic portion are readily soluble and the ampholyte itself only slightly soluble, then naturally the dissociation of the ampholyte and also the solubility will be at a minimum at a definite hydrogen-ion concentration. The p_H that corresponds to this condition is called the isoelectric point. The position depends on the magnitudes of the dissociation constants of the acidic and basic groups. At the isoelectric point we have:

$$[H^+]_{I.P.} = \sqrt{\frac{K_{HA}}{K_B}} \times K_{H_2O}.$$

The position of the isoelectric point is of especially great significance in the study of amino acids and proteins (*cf.* L. Michaelis (27)). P. A. Levene and H. S. Simms (27) give a more complicated formula for $[H^+]$ at the isoelectric point. As to the question of the two isoelectric points of gelatine the reader is referred to the work of J. A. Wilson and E. J. Kern (27); H. P. Highley and J. H. Matthews (27).

7. Minimum Solubility of Difficultly Soluble Electrolytes.—The dependence of minimum solubility on the hydrogen exponent is of great importance in analytical problems. With reference to

the discussion under (6) we see that ampholytes have a minimum solubility at the isoelectric point. If we wish to precipitate these compounds quantitatively we must use a p_H corresponding to the isoelectric point. Aluminium hydroxide falls out most completely between p_H 6 and 7. Hence W. Blum (28) adds methyl red as indicator and adds ammonia until the liquid is just alkaline to the indicator.

As is generally known the solubility of salts of weak acids is largely dependent on the hydrogen-ion concentration. Hence it is easy to understand from the theoretical side that the solubility increases with increasing $[H^+]$. If we call the difficultly soluble salt BA, it is ionized in solution into B^+ and A^-. If we now add hydrogen ions to the solution the following reaction occurs:

$$A^- + H^+ \rightleftarrows HA,$$

thus partially dissolving the salt.

The amount of the salt that dissolves is quantitatively governed by the concentration of the acid added, by the solubility product of BA, and by the dissociation constant of HA.

Similar considerations apply to decomposition of salts by bases.

We will not go further into these analytically important questions here; the reader is referred to the literature (28).

A communication of A. Jung (28) regarding the solubility of uric acid at various p_H-values is of significance. The result is dependent not only upon the p_H but also the kind of buffer mixture with which the test is conducted. Apparently uric acid unites with various anions to form complexes.

8. Tanning.—In common with the action of all enzymes, that of pancreatin toward elastin is dependent on the hydrogen-ion concentration. But the hydrogen exponent at which the decomposition of the elastin is at a maximum depends upon the concentrations of the enzym and the elastin during the reaction. In dilute solution the decomposition takes place only between p_H 7.5 and 8.5, and in concentrated solution between 5.5 and 8.5. We refer to the work of Wilson and Daub (29) for the explanation.

Another question that is connected with tanning procedure is the rate of diffusion of tanning solutions into a gelatine gel. This rate is, according to Wilson and Kern (29), dependent both on the concentration of the non-tannin content and on the p_H. Thus gambier has its greatest penetration capacity at $p_H = 6$; when p_H is smaller than 3, penetration no longer occurs. For quebracho extract the latter limit lies at 4.7; on the other hand it still diffuses rapidly at $p_H = 9$.

The p_H is also of great significance in the analysis of tanning extract by the A.C.L.A. procedure. There is a maximum tannin content at $p_H = 8$ (Wilson and Kern (29)). For further details the reader is referred to the literature (29).

9. Examination of Soils.—In the examination of soils both the p_H of the extract and its neutralization curve are significant. Since many difficulties attend the use of the hydrogen electrode in the measurement of the $[H^+]$ (20), the colorimetric method here gives better service.

It will be shown by a few illustrations that there is a far-reaching connection between the p_H of the soil extract and the occurrence of diseases of various plant growths. Thus peas, for example, have been found to thrive in alkaline but not in acid soils. Conversely the so-called "oat disease of the marsh colonies (Moorkolonien)" does not occur when the reaction is acid.

The crop of clover hay is greater the more the acid reaction of the soil decreases, i.e., the nearer p_H approaches to 7. Thus J. Hudig and C. Meyer (30) give the following data:

Yield of Clover Hay	p_H of the Soil Extract
5.1	5.2
26.4	6.48
25.4	6.48
36.9	7.74
36.8	7.74

According to Gillespie and Lewis (30) the blight of scabby potatoes no longer occurs when the p_H of the soil is lower than 5.16.

From the few data above (*cf.* literature (30) for others) it is clear that in the solution of most problems in the domain of plant pathology the rôle that hydrogen-ion concentration plays in various processes must be carefully considered.

10. Examination of Food and Condiments.—Knowledge of the hydrogen-ion concentration is of importance in judging wine, beer, and fruit juices (31). When these liquids are strongly colored the colorimetric method is not directly applicable. In many cases it is possible to decolorize the solution with charcoal without too far changing the nature of the liquid; the determination may then be made. Knowledge of the p_H of other liquids is also important.

La Mer, Campbell, and Sherman (31) made an interesting study of the rate of destruction of vitamins at various temperatures. They obtained the following results on tomato seeds:

p_H Before Heating	p_H After Heating	Per Cent Destruction of Vitamine
4.3	4.3	50.2
5.2	4.9	58.3
9.2	7.5	61.8
10.9	8.3	63
10.9	8.3	92.5

We may conclude from these figures that the destruction is independent of p_H within wide limits.

Since the action of vitamins decreases more in alkaline than in acid media, McClendon and Sharp (31) call attention to the fact that it is important to know the p_H-values of various food extracts. Various materials have been studied by Clark and Lubs (35) who found the following values:

Substance	p_H at Room Temperature	p_H After Sterilization in an Autoclave
Wheys	1.64–2.56	
Vinegar	2.36–3.21	
Apple juice	3.76–5.65	3.8
Plum juice	4.12–9.44	4.3
Beer wort	4.91–8.55	
Root juice	5.21–9.27	5.2
Cucumber juice	5.08	5.1
French bean juice	5.23–8.63	5.2
Banana juice	4.62	4.6
Potato juice	6.06–9.44	6.1
Sweet potato juice	5.80–8.73	
Maple syrup	6.75–6.8	
Beet juice	6.07–8.75	6.1

They further called attention to the following values in the literature:

	p_H		p_H
Muscle extract	6.8	Grape juice	3.0–3.3
Pancreas extract	5.6	Orange juice	3.1–4.1
Milk	6.6–7.6	Rhubarb juice	3.1
Flour extract	6.0–6.5	Strawberry juice	3.4
Beer	3.9–4.7	Pineapple juice	3.4–4.1
Wine	2.8–3.8	Tomato juice	4.2
Lemon juice	2.2	Plant-cell juice	5.3–5.8
Cherry juice	2.5		

Also McClendon and Sharp (31) determined the p_H of different kinds of juices and found that they were but little changed on boiling; the fluid generally becomes a little more acid.

They give the following data:

Material	p_H Directly	p_H After Boiling
Juice of young roots	5.85	5.80
Potato juice	5.57	
Cabbage	5.90	5.78
Pineapple juice	3.55	3.55
Lemon juice	2.32	2.30

Jenny Hempel (31) found the following figures for lemon juice. Her data for neutralization value toward litmus and phenol phthalein are also given. The latter are expressed in cubic centimeters of 0.2 N alkali per 100 cc.

p_H	Neutralization Number	
	With Litmus	With Phenol Phthalein
2.19	527.7	540.0
2.25	502.1	518.0
2.24	536.0	539.0

Reference is made to the literature (31) for further details regarding the juice of plants and plant cells.

Knowledge of the $[H^+]$ of milk is of special importance both with reference to its daily use, and to dairying. Morres (32) showed that the alcohol test is not sufficient for judging milk. Therefore he adds an indicator, alizarine, at the same time and observes the color. This test is known as the alizarine test. It was unfavorably criticized by Devarda (32). A much better indication of the acidity of the milk is obtained without alcohol. The author uses phenol sulphone phthalein (phenol red), which is colored an acid transition tint by normal milk (cream color verging toward red). With the aid of a color chart the $[H^+]$ of the milk may be found. The color may be judged more readily if phenol red containing a little potassium oxalate is used. The reaction is then more strongly alkaline. Baker and Van Slyke (32) used brom cresol purple as indicator. A drop of saturated

solution of this indicator gives to 3 cc. of milk a grayish blue coloration. This color is brighter if acids are present or if the milk is heated above the Pasteurization temperature. The color is dark blue if water or alkaline salts have been added to the milk, or if it has come from cows with diseased udders (indicating mastitis). In the examination of 350 samples of commercial milk Baker and van Slyke showed that their test of milk was of great value.

Acid or alkali formation may also be shown by brom cresol purple if the specimen is allowed to stand for twenty-four hours in a sterile tube.

The nature of the results of baking depends upon the p_H of the original dough. An important investigation in this field was made by H. Jensen-Hansen (31), whose results will be briefly described. For every dough made from white flour there is an optimum p_H at which the bread baked from the dough will have the best properties. This optimum is about in the neighborhood of $p_H = 5$; for good flours the p_H lies at a higher and hence the hydrogen-ion concentration at a lower value; conversely, dough from poorer flour has an optimum p_H at a lower value; hence Hansen found for dough made from dawn-red wheat an optimum at p_H 5.85 (the density of the bread was 2.92), from oceanic wheat at p_H 4.70 (density of bread 2.80). The kind of acid with which the dough is brought to the desired p_H has little influence on the nature of the bread. The means that are used to increase the quality of the bread, such as salts of aluminium, zinc, copper, and primary phosphate, all increase the acidity of the flour, a circumstance to which their favorable action must be ascribed.

E. J. Cohn, P. H. Cathcart and L. J. Henderson (31) give a practical test that depends on the acidic properties of bread. We may call it the "methyl red reaction" for bread. The p_H of suspension of bread may be found by means of methyl red; it is simpler to let a drop of the indicator fall on a slice of bread and compare the color with an established scale for methyl red. Each transition tint corresponds to a definite p_H. The color of the bread extract treated with the indicator changes

proportionately to that of the slice of bread on which the indicator is dropped.

They cut the bread freshly before performing the test and immediately allow 4 drops of 0.02 per cent methyl red in 60 per cent alcohol fall on a spot near the middle of the slice. The color is judged after five minutes. The p_H of good bread lies in the neighborhood of 5.4. For further details the reader is referred to the literature (31).

The acid taste of wine, etc., is in large measure dependent upon the hydrogen-ion concentration. With some practice it is possible to deduce the approximate hydrogen-ion concentration of wine from the taste. For details see the work of Th. Paul (31).

11. Sugar Industry (33).—An interesting investigation was recently published by J. F. Brewster and W. G. Raines (33). If the sugar juice is only purified with lime the best precipitation of the impurities results at neutral reaction, $p_H = 7.0$. The reaction may be tested suitably against methyl red using buffer mixtures. It is possible to get along without buffer mixtures by adding lime until brom cresol purple is alkaline and then enough more to bring the titration acidity down to 0.25–0.50 cc. N acid per 100 cc. of juice.

If the juice is to be treated with sulphurous acid for bleaching purposes this is best done at p_H about 3.8 (tested against methyl orange) and at a titration acidity of 5. Then enough lime is added to bring the p_H to 7.

The following example gives an expression for the buffer capacity of cane sugar. The titration acidity is expressed in cubic centimeters of 0.1 N sodium hydroxide per 10 cc. of juice neutralizing to phenol phthalein. The amount of lime added is in cubic centimeters of 0. 0.1 N per 10 cc. of juice.

Acidity.....	10.25	9.40	8.85	7.95	7.00	5.50	4.75	4.00	2.80	2.00	1.30	0.70	0.00
Lime added..	0.00	0.85	1.40	2.30	3.25	4.75	5.50	6.25	7.45	8.25	8.95	9.55	10.25
p_H.....	3.0	3.4	3.4	3.6	4.5	5.4	5.6	5.8	6.0	6.4	6.8	7.4	8.4

The hydrogen exponent is significant for the process of decolorization of sugar juice by charcoal; e.g., see Turrentine

and Tanner (33). According to Brewster and Rainer (33) the decolorizing action of charcoal increases as the hydrogen-ion concentration rises between the limits p_H 4 and 8.

12. Pharmacy (34).—R. L. Levy and G. E. Cullen (34) looked into the decomposition of crystalline strophanthin in aqueous solution. In sterilizing the solution they found that alkali from the glass often caused the p_H to rise from 6 to 9. (This does not happen in Jena glass.) For clinical purposes it is best to dissolve the strophanthin in an 0.02 molar phosphate buffer of p_H 7.0 and sterilize.

Macht and Shohl found that the stability of benzyl alcohol is strongly decreased by traces of alkali; hence it must be sterilized in good glass.

A. Rippel (34) found that some alkaloid salts are decomposed on sterilizing, especially in alkaline solution.

J. R. Williams and M. Swett (34) made an investigation of the p_H of distilled water, physiological salt solutions, glucose and other solutions for injection into the blood stream and showed that too little attention had been paid to the p_H of such solutions.

According to the findings of the Mulford Biol. Lab. (34) salvarsan, i.e., the hydrochloride of diamino-diazo-arseno benzene, has an acid reaction in solution, the p_H being 4.8. The solution must be neutralized before it is injected. With two equivalents of alkali the free base precipitates and with three the monosodium salt is formed, with four the soluble disodium salt of $p_H = 9.4$ in solution; the latter is suitable for injection.

13. Biochemical, Bacteriological, and Physiological Investigations.—The hydrogen-ion concentration plays an important rôle in all biochemical and physiological processes. Enzymes and bacteria have an optimum action at a definite p_H. Proteins are completely coagulated at a certain $[H^+]$ (the *isoelectric point*) or *change the sign of their electrical charge*. The $[H^+]$ of body fluids, as urine, intestinal fluid, contents of stomach, blood, varies between very narrow limits under normal conditions. In many cases of this sort use may be made of the colorimetric method. Because of the great extent of the subject and the extensive literature (35) thereof it will not be possible to treat it further

here. Especial attention is called to the fact that Clark (35) in his book has a complete bibliography dealing with the significance of p_H in the various branches of chemistry and especially of biochemistry.

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CHAPTER VII

INDICATOR PAPERS

1. Use of Indicator Papers.—Such papers serve the purpose of showing the reaction of a liquid, just as indicators do. As we shall see, the sensitivity of these papers is influenced by so many factors that it is not in general possible to use them in determining hydrogen-ion concentration exactly. The p_H of buffer mixtures may be approximately determined with indicator papers (see p. 226). Their use is often to be recommended for qualitative purposes; for instance, for testing gases for acidic or basic components (ammonia, acetic acid, etc.). Reagent papers are useful in testing qualitatively for metals. For certain operations $[H^+]$ should be between definite (although wide) limits. Thus the hydrogen-ion concentration should be about 0.02–0.05 N during the precipitation of the copper group to insure complete precipitation of cadmium and lead and no precipitation (or at most a trace) of zinc. This degree of acidity may be established with the aid of methyl violet paper. Further, the precipitation of basic acetates and formates of iron, aluminium, and chromium requires a $[H^+]$ of 10^{-5} to 10^{-6}. The solution under examination is neutralized until it is no longer acid to congo paper, but still acid to litmus. Indicator papers are useful in tests for the identification of pharmaceuticals. Strong mineral acids react acid to methyl violet paper, moderately strong acids to congo paper, and very weak acids to litmus or azolitmin paper. Strong bases react alkaline to turmeric or tropeolin 00 paper, moderately strong bases to phenol phthalein paper, and very weak ones to litmus or azolitmin paper. Indicator papers are not very generally used in quantitative analysis, nor are they to be generally recommended for such use (1). It is not possible to use

indicator solutions with strongly colored solutions like fruit juices, wine, etc., and papers also usually give results that are not clear-cut. This is especially true if the solution that is being titrated contains buffer mixtures at the point where the indicator begins to change color. In such instances it is better to use other methods (hydrogen electrode, conductometric, or spectroscopic (2)). Indicator papers can not be recommended for the determination of weak acids (like acetic) in presence of strong ones. According to Glaser's findings (3) the change is not sharp.

2. Sensitivity of Indicator Papers.—The sensitivity depends on various factors that will be discussed in greater detail. It should be noted that the sensitivity is always less than with indicator solutions. If buffer mixtures are used reagent papers show the same sensitivity as the corresponding solutions of indicators.

(*a*) *Kind of Paper.*—Sized papers in general show sharper reactions than filter paper because the drops of liquid used in the test are not so strongly absorbed and the change is confined to a smaller space. If the liquid to be tested is colored, filter paper is to be preferred, especially if the color of the solution and that of one form of the indicator are the same. The paper causes, by capillary action, a separation of the coloring matter and the colorless fluid if the colored matter is of basic character. The change appears at the rim of the drop in such cases. The sensitivity of sized paper is much less than that of filter paper as Kolthoff (4) has shown. The reason is apparently that sized paper takes up less of the indicator. The sensitivity of some sized papers is given in the following table (+ signifies feeble reaction; − no reaction).

Sensitivity of Sized Papers

Indicator	10^{-3} N HCl	5×10^{-4} N HCl
Congo	+	−
Dimethyl amino azo benzene	−	−
Litmus (very weakly colored)	+	−

(*b*) *The Nature of Pre-treatment of the Paper.*—Because of the colloidal nature of many indicators study was made of the effect on the sensitivity of pre-treatment of the paper with various reagents, as hydrochloric acid, aluminium chloride, sodium hydroxide, etc. After treatment with hydrochloric acid or aluminium chloride the washing was continued until the water no longer reacted acid to methyl red; if treated with alkali the washing was continued until the water was no longer alkaline toward phenol phthalein. Paper of various kinds thus treated was immersed in solutions of congo red, methyl yellow, azolitmin and phenol phthalein (see section 4 following). It was found that the pre-treatment was practically without effect on the sensitivity if pure paper, was used. If this is not pure, treatment with hydrochloric acid is sufficient. The kind of filter paper is of little significance, although the Schleicher and Schüll paper "for capillary analysis" was found to be most sensitive. The difference is so small that practically no attention need be paid to the kind of paper.

(*c*) *Concentration of the Indicator in the Paper.*—Just as in case of indicator solutions the concentration plays an important rôle here also. If we consider an acid indicator, HIn, it may be found simply (*cf.* Chap. III, page 55) that:

$$[H^+] = \frac{[HIn]}{[In^-]} K_{HIn}.$$

In the case of the congo-acid [HIn] represents the concentration of the blue form and $[In^-]$ that of the red. If we compare two congo red papers of which one contains ten times the congo red concentration of the other, then at the same $[H^+]$ one will contain ten times the [HIn] concentration of the other. If the acid, i.e., blue form is readily detected in the presence of In^-, the concentrated paper will be more sensitive toward acid than the more dilute. This is not generally true but depends upon the sensitiveness with which the acid form may be recognized in presence of the basic. Similar considerations apply to basic indicators. These remarks apply only when the papers

have been prepared from pure indicator solutions. This is not the case, for example, with red and blue litmus paper. Blue litmus paper contains an excess of base, red paper of acid. It is thus obvious that these papers at a given concentration of coloring material will show the H^+ or OH^- the more sensitively the more dilute the solutions used in their preparation. This holds only partly for violet litmus, which contains some ampholyte.

The effect of the concentration of congo red on the sensitivity of the paper is given in the following table.

Concentration of the congo solution with which paper is saturated	0.01 N HCl	0.005 N HCl	0.001 N HCl	0.0005 N HCl	0.0002 N HCl	0.0001 N HCl
1%	+++ Intense blue spots	+++ Intense blue spots	+++ Spots	+	+	−
0.1%	+++ Deep blue spots	+++	++ Blue circle red in center	+	+ Pale	−
0.01%	+	+	±	−	−	−
0.001%	−	−	−	−	−	−

This table shows that the most sensitive congo paper is obtained by soaking the paper in 0.1 or 1 per cent solution. The sensitivity then extends to 0.0002 N HCl. 0.1 per cent paper is generally to be recommended because the color change is easy to see.

The sensitivity of litmus and azolitmin papers increases as the concentration becomes smaller. This is clear from the following table. The ordinary paper is prepared using a 1 per cent solution.

EFFECT OF CONCENTRATION OF LITMUS OR AZOLITMIN ON THE SENSITIVENESS OF THE PAPER

Description of Paper	Concentration of HCl				
	10^{-3} N	5×10^{-4}	2×10^{-4}	10^{-4}	5×10^{-5}
Blue litmus 1%	++	−	−	−	−
Blue litmus 0.1%	+++	++	+	−	−
Violet litmus	+++	++	±	−	−
Azolitmin 1%	+++	+++	++	++	−
Azolitmin 0.1%	+++	+++	++	++	−

Description of Paper	Concentration of NaOH			
	10^{-3} N	4×10^{-4} N	2×10^{-4} N	10^{-4} N
Red litmus 1%	++	++	+	−
Red litmus 0.1%	++	++	+	−
Violet litmus	++	++	+	−
Azolitmin 1%	+++	+++	++	+
Azolitmin 0.1%	+++	+++	++	+

In determinations of the sensitivity with alkali, pure water entirely free from carbon dioxide should be used, for otherwise a smaller sensitivity is found than really exists.

From these experiments it follows that *the most sensitive reagent for strong acids and bases is azolitmin paper prepared from* 0.1 *per cent solution.* The presence of 10^{-4} N hydrochloric acid or sodium hydroxide may be proved with this paper. It is also the best paper for weaker acids or bases.

The same considerations apply to methyl violet paper as to litmus. If it is prepared from concentrated solution it may scarcely be used. The color of the paper should be bright violet; it is prepared by using an 0.04 per cent methyl violet solution. 0.01 N hydrochloric acid just colors the paper violet blue, 0.1 N HCl bluish green, and 1 N HCl yellowish green.

Phenol phthalein paper acts differently from the other two papers. It is indifferent as to whether the paper is pre-treated or

not, for drops of liquid remain lying on the paper and diffuse in only very slowly. 1 and 0.1 per cent alcoholic solutions are used in preparing the paper. Apparently these concentrations are so high that the indicator crystallizes out in the pores of the paper during the drying. Because of the slow diffusion of liquid into the paper it requires a moderately long time before an alkaline reaction is evident. The result may be obtained more rapidly by aiding the contact between liquid and paper by means of a rod. The phenol phthalein then dissolves.

The reaction then takes place in the drop and not in the paper; it might rather be allowed to take place in a capillary tube. The sensitivity of phenol phthalein paper is the same as that of the solution, as may readily be understood. An 0.0001 N sodium hydroxide solution gave a pale rose coloration with the paper. The advantage of phenol phthalein paper is that no capillary phenomena take place which makes the test sharper. The drops diffuse in only after some time and then finally the rose or red color disappears.

The concentration of indicator plays a rôle in other instances. The most satisfactory concentration of indicator is given in the table at the end of this chapter (page 230).

(*d*) *Manner of Using the Reaction.*—Ordinarily a drop of the solution to be tested is placed on the paper. The paper may also be dipped into the solution. The latter does not offer much advantage. The author found that the sensitivity was always less than when the drop was placed on the paper. Besides, you have to observe quickly because of capillary phenomena that cause the indicator to diffuse away. On long immersion a part of the indicator dissolves, the process being hastened by electrolytes (Walpole (5)).

(*e*) *Nature of the Solution.*—Up to the present we have been considering the sensitivity of the indicator toward strong acids or bases. Except in the case of phenol phthalein the sensitivity is greater with solutions than indicator papers. If we compare, for example, an 0.0001 N hydrochloric acid solution with a mixture of about 90 cc. 0.1 N acetic acid plus 10 cc. of 0.1 N acetate, both solutions give about the same color with methyl yellow. If

the test is made with azolitmin paper, the acetic acid-acetate mixture reacts apparently more strongly acid than the hydrochloric acid; it therefore follows that *an indicator paper does not show the true acidity, or hydrogen-ion concentration, very well.* If hydrogen-ions are removed in any way (by absorption by paper or impurities in the paper or indicator) no H-ions are supplied. The liquid appears to be neutralized. If a buffer mixture is used traces of impurities are without effect. If the sensitivity of indicator papers is examined with buffer mixtures it is found to be the same as that of indicator solutions. *With strong electrolytes, indicator papers give more nearly an expression of titration acidity than of hydrogen-ion concentration.*

A paper that in some degree gives both a measure of titration acidity and H-ion concentration is potassium iodide-iodate paper. Iodide and iodate react according to the equation:

$$5I^- + IO_3^- + 6H^+ \rightleftarrows 3I_2 + 3H_2O.$$

This is a time reaction whose speed is very largely dependent on the $[H^+]$. From the equation it is evident that the $[H^+]$ decreases as a result of the reaction. If we again compare 0.0001 N HCl with the acetic acid-acetate mixture both give instantaneously the same brown or blue color. The paper treated with the buffer mixture gradually becomes darker because the $[H^+]$ removed is gradually re-supplied. This does not occur with the hydrochloric acid.

3. Determination of Hydrogen-ion Concentration with Indicator Papers.—We have seen in the preceding pages that indicator papers give about the same transition range as solutions with buffer mixtures. *In the presence of a sufficient amount of buffer the hydrogen exponent may be quite exactly determined.* Fräulein Hempel (6) investigated this matter at the suggestion of Professor Sörensen; she found lacmoid paper useful between p_H 3.8 and 6.0. A drop of the solution was brought on to the paper and the color was compared with that caused by buffer mixtures. The accuracy amounted to about 0.2–0.5 p_H. Haas (7) has extended the procedure. He gives directions for the preparation of blue and red lacmoid paper. One drop of the

unknown solution is placed upon each of several strips of the paper. At the same time a series of comparison papers of known $[H^+]$ is made with buffer mixtures. The strips are slowly dried over soda-lime (to exclude carbon dioxide). During the drying the colors are compared now and then; the actual determination is made when the strips are entirely dry. The middle portions of the drops are compared, the color at the rims being generally effaced by diffusion. A series of more stable reference papers may be made by covering the paper with good paraffin. Haas used indicators other than lacmoid paper:

Methyl orange paper	for p_H 2.4–3.8
Brom phenol blue paper	for p_H 3.4–4.6
Alizarin paper	for p_H 4.0–6.0
Azolitmin paper	for p_H 6.2–8.0
Neutral red paper	for p_H 7. –9.

The accuracy of the procedure according to Haas varies from 0.4 to 0.2 p_H. The procedure may be used with advantage in the determination of p_H in small quantities of liquid. *Great care is necessary in using the method.*

The author has also investigated the procedure of determining p_H with indicator papers. The results will be described briefly here. In opposition to Haas it was found that the drops should not generally be allowed to dry, for the color then becomes very indistinct and slight differences are difficult to recognize. Furthermore it is better to bring the drops to the paper with a capillary than with a glass rod. Thus only 10–20 mm. of liquid suffice. It is generally best to use hardened filter paper; also Schleicher and Shüll's paper for capillary analysis is often very suitable. The " intensity " of buffer action is very important. If, for example, a phosphate mixture of $p_H = 7.0$ is diluted tenfold and the color judged with red litmus paper the original solution is apparently more strongly alkaline than the diluted solution. It is recommended that buffer solutions of about the same buffering power as that of the unknown solution be always used for comparison purposes. The accuracy of the procedure is then about 0.2 p_H. The procedure may be of importance in

the rapid testing of blood serum and urine. If the solution under examination contains very volatile acids (e.g., carbonic) and a negligible amount of non-volatile ones the procedure can not be used.

The reader is referred for details to Kolthoff (8). In the table are given the indicator papers that the author has found to give good service.

Kind of Paper	Concentration of Indicator Solution	Useful between p_H	Time to Wait after Applying Drop	Accuracy, and Remarks
Congo red (hardened paper)	0.1%	2.5– 4	Less than 5 minutes	About 0.2 p_H. On drying the blue spot again becomes red.
Methyl orange	0.2%	2.6– 4.0	After 2 minutes	About 0.2 p_H, must be judged rapidly. Congo paper generally better; effect of dilution large.
Alizarine (hardened paper)	0.1%	4.6– 5.8	After 5 minutes	About 0.2 to 0.3 p_H.
Blue lacmoid paper	.....	4.6– 6.0	After 5–10 minutes	0.2–0.3 p_H.
Brilliant yellow	0.2%	6.8– 8.5	After 5–60 minutes	0.2 p_H. Can not be allowed to dry when boric acid is present (in buffer mixture).
Red litmus	.....	6.6– 8.0		
Blue litmus	.....	6.0– 8.0	After 5–60	0.2 p_H. Can not be allowed to dry
Azolitmin	1%	5.5– 8.0	minutes	when boric acid is present.
Phenol red paper	0.1%	7.0– 8.2	After 2–30 minutes	0.2 p_H.
Cresol red paper	0.1%	7.6– 9.0	After 2–30 minutes	0.2 p_H.
α-Naphthol phthalein paper (capillary)	0.2%	8.2– 9.5	After 5 minutes	0.2 p_H.
Curcuma paper	0.1%	7.5– 9.5	After 10 minutes	0.2 p_H. Can not be allowed to dry if boric acid is present.
Thymol phthalein paper	0.1%	10 –11	After 2 minutes	

4. Capillary Phenomena of Test Papers.—Capillary phenomena of filter paper have often been studied. They must be taken into account in testing reactions with indicator papers, especially as the limit of sensitivity of the paper is approached. If a drop of 0.001 N HCl is allowed to fall on congo red paper the center of the diffusing drop remains red, i.e., alkaline and is surrounded by a circle of acid and further out a circle of water. Similar phenomena are given by methyl yellow, azolitmin, litmus,

and other papers. The ratio between the radii of the water and acid circles depends in a definite way on the hydrogen-ion concentration (*cf.* Holmgren and other investigators (9)). The following is the explanation of the formation of circles: The whole portion of the paper out as far as the acid circle is acid, but to such a slight extent in the center that the $[H^+]$ is not large enough (taking congo paper as illustration) to form the blue acid. Upon putting the drop on the paper the water diffuses more rapidly followed by the very mobile hydrogen ions. Hence at a definite distance from the center the difference in concentration from that of the original solution is large enough to form the acid modification of the indicator. The acid circle acts as a chemical filter and only allows water to pass.

Capillary phenomena may arise from other causes. A solution of ammonium acetate colors both red and blue litmus paper violet. Yet it is plain that the drop is more blue at the center and more red at the rim. The ammonia is more strongly held by the paper than the acetic acid. The phenomena are more marked if the reaction of lead acetate is tested. At some distance from the center there is first formed a blue circle (absorption of lead hydroxide), around which is formed a red ring due to diffusion of acetic acid. This behavior gives an explanation of the contradictory statements in various pharmacopœias regarding the reaction of lead acetate. The reaction of this salt can not be established certainly with litmus paper; it should be done with the aid of methyl red solution. The acid or alkaline reaction of salts such as sodium acetate or ammonium chloride that are hydrolyzed may be easily shown with indicator papers.

5. Preparation of the Papers.—According to Glaser, indicator papers are prepared as follows: Strong white filter paper is purified by treatment with hydrochloric acid and ammonia, and then with distilled water, and dried. Glaser found that Schleicher and Shüll No. 595 paper was best adapted. The dried paper is soaked with the indicator solution. If white sized paper,—a good grade of writing paper being best,—is used, the solution is brushed on. The moist paper is dried best by suspending it with threads and wax, and being careful to secure uniform distribution of the

color by changing the position of the paper frequently. The drying must be done in a room free from acid or alkaline fumes.

Blue litmus paper may best be made according to Glaser (3) (page 70) by first extracting the litmus cakes with alcohol. The residue is dried and extracted with cold water. Filter paper is saturated with the aqueous solution and dried. The free alkali is removed by washing with water, most conveniently on a glass plate. (The excess of acid or alkali can be removed better before the paper is saturated with the solution.)

TABLE OF SENSITIVITY OF INDICOTOR PAPERS.

Kind of Indicator	Concentration of Indicator Solution with which Paper is Saturated	Sensitivity to		Remarks
		HCl	NaOH	
Haematoxylin	0.2%	0.2–1 N	.....	From yellow to beautiful cherry red.
Methyl violet	0.4%	10^{-2} N	.....	Blue with 10^{-2}HCl, blue green with 10^{-1}; greenish yellow with N.
Methanil yellow	0.2%	5×10^{-3} N	.....	Yellow-red.
Tropeolin 00	0.2%	4×10^{-3} N		
Methyl yellow	0.2% in alcohol	4×10^{-4} N		
Congo red	0.1%	2×10^{-4} N		
Blue litmus	1.0%	10^{-3} N		
Blue litmus	0.1%	2×10^{-4} N		
Violet litmus	1%	4×10^{-4} N	5×10^{-5} N	
Red litmus	1%	.....	2×10^{-4} N	
Red litmus	0.1%	.....	10^{-4} N	
α-Naphthol phthalein	0.1%	.....	5×10^{-5} N	
Brilliant yellow	1%	.....	10^{-5} N	Yellow—Red brown ↓ ↓ acid alkaline
Phenol red	0.1%	.....	5×10^{-5} N	Yellow—Red ↓ ↓ acid alkaline
Cresol red	0.1%	.....	5×10^{-5}	Yellow-purple red
Phenol phthalein	1%	.....	5×10^{-5}	
Phenol phthalein	0.1%	.....	10^{-4}	
Turmeric (curcuma)	0.2%	.....	10^{-3}	Yellow—Red brown ↓ ↓ acid alkaline
Thymol phthalein	0.1%	.....	10^{-3}	Colorless-blue
Tropeolin 0	0.2%	.....	3×10^{-3}	Yellow—Red brown ↓ ↓ acid alkaline

Red litmus paper may be made, according to Glaser, by using acid tincture or by dipping the blue paper in dilute sulphuric

acid and then washing with distilled water. It may be prepared better by using the aqueous solution that is used in preparing the blue paper. This is also described by Fresenius and Grünhut (10). The aqueous solution is treated with sulphuric acid until the color is barely red. The paper is saturated with this solution. Fresenius and Grünhut boil the solution for fifteen minutes replacing the water that evaporates. If the red tint again changes to violet it is again treated with sulphuric acid and the process continued until the desired tint is obtained. The violet paper is better to use than either red or blue because it shows both alkaline and acid reaction. The aforementioned aqueous solution of purified litmus is brought to the right tint with acid and the paper is then saturated. Pure preparations should be used in the preparation of the other papers. All indicator papers must be protected from air and light. Light decolorizes most papers.

6. Limits of Sensitivity of Indicator Papers.—The sensitivity is given only for those papers that are practically useful. The author has made experiments with lacmoid,—*p*-nitro-phenol 1 per cent and 0.1 per cent,—neutral red, methyl red, and other papers, but the color change was not sharp enough.

The papers in the table were made from ordinary filter paper which was saturated with indicator solutions of the concentrations given.

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CHAPTER VIII

THEORY OF INDICATORS

1. Theories of the Color Change.—There are two views upon the question of what chemical changes occur to give rise to the color change: The *ionic theory*, or the theory of Wilhelm Ostwald (1) and the **chromophoric** or *chemical theory* that is ordinarily called the Hantzsch theory. In addition to these two theories, Wolfgang Ostwald (2) introduced a new point of view a few years ago. He maintained that the color change is related to a change in degree of dispersion of the indicator. It follows from the work of Kruyt and Kolthoff (3) and others that this is not always the case, so that Wolfgang Ostwald's view is not of general validity. Even if the degree of dispersion did change with the color it might not be the cause of the change, but merely a parallel phenomenon; furthermore it is difficult to see why only hydroxyl and hydrogen ions should have such a large influence on the degree of dispersion and color. Therefore we shall disregard the conception of Wo. Ostwald in discussing the theories of indicators. Hence there remain the theories of Wm. Ostwald and of Hantzsch to discuss. According to Ostwald indicators are weak acids or bases whose undissociated form has a color different from that of the ions; in other words, Ostwald ascribes the color change to transformation into ions or the reverse. The indicator HIn is ionized in aqueous solution as follows:

$$HIn \rightleftarrows H^+ + In^-,$$

$$\frac{[H^+][In^-]}{[HIn]} = K_{HIn},$$

$$\frac{[In^-]}{[HIn]} = \frac{K_{HIn}}{[H^+]}.$$

$\frac{[In^-]}{[HIn]}$ signifies nothing else than the ratio of the amount of alkaline to that of the acid form.

This gives directly the manner in which the color changes as $[H^+]$ becomes larger or smaller (see Chapter III). The great advantage of the Ostwald view is that we may use it in the quantitative study of the change. Although the original view of Ostwald is not entirely correct, the equation given may be steadily applied in case the acid is monobasic. Ostwald later attempted to formulate his theory more acceptably. He showed that all salts of a colored anion with colorless cations or vice versa, had the same color (e.g., permanganates, chromates, etc.). In some cases discrepancies were found. The anomalies in case of copper and cobalt salts disappear on dilution. Complex ions are present in more concentrated solutions, but are dissociated into simpler ions on dilution. An exact study that Ostwald made of 300 salts apparently completely established his theory. That electric charge causes color is shown by so-called " ion isomerism " i.e., the same substances in differently charged conditions have different colors, e.g., ferrous and ferric iron, manganate and permanganate, etc.

Many objections have, however, been raised against the Ostwald theory; a review of these is given in a monograph by Thiel (4). Since many of these objections have been overcome, only a few will be considered with brief discussion of their merits:

(*a*) If a little alkali is added to phenol phthalein the solution becomes red, but upon adding more alkali the color fades. This anomaly is explained by Ostwald on the basis of formation of other ions.

(*b*) The solid salt of phenol phthalein is red. It can scarcely be assumed that the solid salt of phenol phthalein is dissociated so that it should be colorless according to Ostwald's theory. The same is true of the solid salt of *p*-nitro-phenol. *p*-Nitro-phenol is colorless in acid solution, and yellow in alkaline. The solid salt should be colorless, being undissociated; as a matter of fact it is colored (see page 246).

(*c*) The most important objection to Ostwald's conception is

that several color changes are very plainly time reactions; this is true for example of tropeolin 000 (Handa (5)), Haematein (Salm and Friedenthal (6)), and phenol phthalein[1] (Wegscheider (7)). If the change were to be ascribed to the direct passage of undissociated acids into ions the change should occur at once for most ionic changes are almost instantaneous. The slow change indicates clearly that molecular reactions are occurring.

(*d*) Hantzsch (8) and Hantzsch and Robertson (9) studied the relation between the concentration of colored electrolytes and Beer's law. Beer's law held exactly for colored salts even though the concentration was altered through a wide range. The law was also found to apply to solutions in non-aqueous solvents such as methyl alcohol, ethyl alcohol, pyridine, acetone, amyl alcohol, and concentrated sulphuric acid. If the ions had a color different from that of the undissociated substance this could not hold, since in non-aqueous solutions especially, the degree of dissociation is strongly altered by change in concentration. They thus proved that the ions and the undissociated compounds had the same color. This conclusion does not agree with the series of investigations that were carried out by H. C. Jones and his collaborators.

From the evidence cited it follows that Ostwald's theory in its simple form can no longer be regarded as the explanation of the change of indicators. It has at present been replaced by the chromophoric theory, although the author wishes to call attention to the fact that the latter theory in itself is not an explanation of the color change, but merely calls attention to a fact that occurs at the same time as the color change.

2. The Chromophoric Theory.—The source of the theory may be traced back to Bernthsen (10) and Friedländer (11) who almost simultaneously, and independently, showed that phenol phthalein in acid solution is colorless and has a lactone structure, and forms a red salt in alkaline solution that is not derived from a phenol, but has a chromophoric quinone group. The color

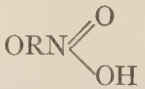
[1] The slow color change of phenol phthalein is to be ascribed to the carbonic acid content of the solution. If the solutions are free from carbon dioxide the color change is sharp and the color does not change on standing.

change is here accompanied by alteration in constitution. Later chiefly Hantzsch and his pupils worked out the theory and found that the constitution changes with every change in color, and that if the constitution remains unchanged the color is unaltered. It should be pointed out that complete and sharp proof has not been found in all cases since proof of change in constitution is at times accompanied with very great difficulties.

The relation between color and constitution has been shown by Hantzsch and his collaborators especially for the nitro-paraffins and the nitro-phenols. These substances are yellow in alkaline solution and colorless in acid. Hantzsch et al. showed that the formation of the salt from the acid and vice versa is a slow time reaction. If a solution of the salt was treated with an equivalent amount of acid the color remained strong yellow and the conductance was high. The latter proved that a strong acid was present in the solution. The longer the solution stood the weaker became the color and at the same time the conductance decreased until finally both color and conductance remained constant. The strong acid had therefore gone to form neutral material (or a weaker acid), or in other words we have here a case of the formation of a *pseudo*-acid, or *aci*-combination. A strong acid that is formed from a substance that is not itself an acid, or at most a weak acid, by molecular rearrangement is called an *aci*-compound. The salts and esters derived therefrom are called *aci*-salts and *aci*-esters. The substance from which the *aci*-compound is formed is called a *pseudo-acid*. In the same way we speak of *pseudo-bases* and *baso*-compounds.

The aci-compound of phenylnitromethane, therefore, goes over slowly in acid solution to form a pseudo-acid. At the same time the color changes from yellow to almost colorless.

Hantzsch showed that the aci-compound generally has the following constitution:



aci-compound, yellow

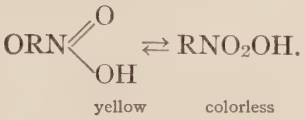
while the pseudo-compound had the following structure:

RNO_2OH

pseudo-compound, colorless

Now it was found that the aci-form is not completely transformed into the pseudo-form in acid solution, but that equilibrium is finally established between the two forms:

aci $\rightleftarrows$ pseudo, or

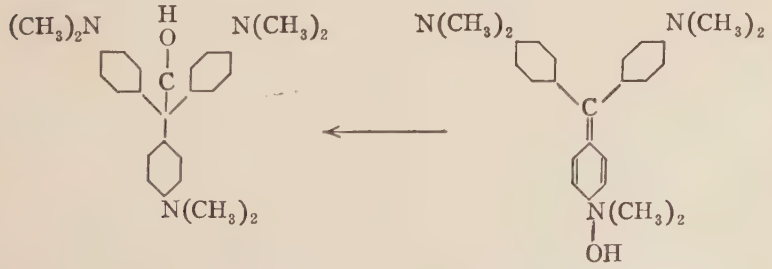


When alkali is added the aci-compound is transformed into aci-salt, and the equilibrium is displaced to the left and the color becomes more yellow.

Hence it follows that on transformation into the salt form no ions of the colorless pseudo-compound are formed, but it is first rearranged into the aci-compound and colored ions are formed from the latter.

Hantzsch further afforded proof that these aci- and pseudo-compounds are really formed because he prepared esters of both that were yellow and colorless respectively.

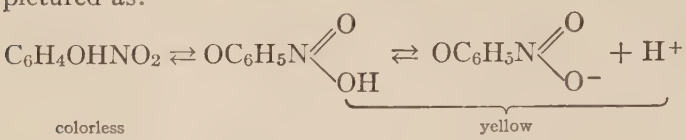
Hantzsch likewise explained the relation between *pseudo-bases* and *baso*-compounds. If a salt of crystal violet is made alkaline the violet color appears and the conductance is high. On standing, the solution becomes colorless and the conductivity falls to a low value. The baso-compound which is a strong base and is violet colored has a different constitution from the colorless pseudo-compound:



pseudo-crystal violet base; gives nearly neutral solution.

baso-compound, violet; gives strongly alkaline solution.

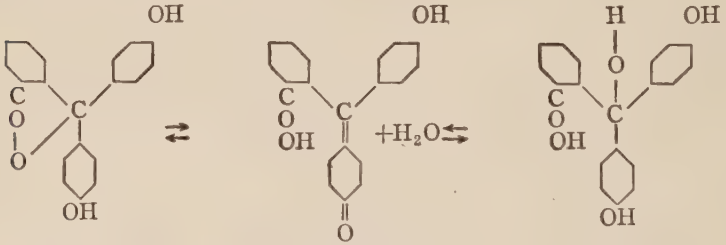
3. Color Change of Indicators According to the Chromophoric Theory.—*p-Nitro-phenol.*—On this theory the color change is pictured as:



The equilibrium shifts toward the right when alkali is added.

Phenol Phthalein.—Phenol phthalein is taken as a model for the phthaleins which in general behave in similar manner.

Phenol phthalein itself is colorless and has a lactone structure. On going over into its salt form, its constitution changes to that of a quinone compound. If a very large excess of alkali is added the quinone is transformed into the salt of a colorless phenol carobyxlic acid. The changes are represented by the following formulas.



lactone: colorless, acid

quinone: red, feebly alkaline

carboxylic acid: colorless, strongly alkaline.

At slight alkalinity we have to deal only with the lactone and quinone forms. The latter acts as a strong acid. Upon adding alkali the quinoid salt is formed and the equilibrium is displaced toward the side of the red components. (See also the work of Acree and his collaborators on the constitution (1917; 1918; 1919).)

The reader is referred to the work of Clark (1922) for theories of the color change of the sulphone phthaleins.

Dimethyl Amino Azo Benzene.—This indicator is chosen as a representative of the azo-series of indicators; it is yellow in alkaline solution, having then the azo-structure, and red in acid

media, when its structure is of the quinoid type. Many other formulas have been suggested, especially for methyl orange, but these will not be considered here. The simplest way to picture the color change is as follows:

azo form: yellow: very feebly basic, or neutral

quinoid form: red: strong base

Hence if an alkaline solution of the indicator is acidified the equilibrium is displaced toward the right since the quinoid form is transformed into a salt.

4. New Definition of Indicators.—It is quite evident from the preceding pages that the simple explanation of Ostwald can no longer be regarded as correct. On the other hand it is not possible to explain the relation between the color (or ratio of acid and alkaline forms) and hydrogen-ion concentration as simply due to alteration in constitution alone. Stieglitz (12) has established a compromise between the ionic and chromophoric theories that makes it possible to calculate the relation between color intensity and hydrogen-ion concentration using the Ostwald equation. Yet he rejects the theory of Ostwald as an explanation of the change because it gives no reason for the *alteration in color*, and adopts the chromophoric view. The author's view is somewhat different. The chromophoric theory gives *no explanation of the change, but calls attention to a phenomenon that accompanies the color change. The color change is accompanied by a change in constitution, but this is not the cause of the color change.*

The above statement does not detract from the beautiful work of Hantzsch, which is of great significance for organic chemistry. Yet change in constitution is not to be regarded as the reason that the color changes. Although the color change is easy to perceive and the change in constitution difficult, the two

phenomena occur simultaneously. If, conversely, the change in constitution were easy to perceive and the color difficult, the latter would not be regarded as the reason for the change in constitution. Besides, it is hard to see on the basis of the Hantzsch conception why the hydrogen-ion concentration governs the change of an indicator.

Hence we have come to the question: What determines the color of an indicator?—The answer is simply: *The equilibrium that exists between the aci- or ionogenic form and the pseudo- or normal form.*

If we again start with *p*-nitro-phenol as illustration, then in aqueous solution there is an equilibrium between the aci- and pseudo-forms as pictured by the equation:

$$\text{normal} \rightleftarrows \text{aci.}$$

When equilibrium is established the following relation holds:

$$\frac{[\text{aci}]}{[\text{normal}]} = K. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$[\text{aci}] = K \times [\text{normal}]. \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The aci-form behaves as a strong acid and is converted into salt by alkali:

$$\text{aci} \rightleftarrows H^+ + A^-$$

$$\frac{[H^+][A^-]}{[\text{aci}]} = K_{\text{aci}}. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

This K_{aci} represents the dissociation constant of the aci-acid. Now it follows from equation (2) that the concentration of the aci-acid is equal to $K \times [\text{normal}]$, or in other words:

$$\frac{[H^+][A^-]}{[\text{normal}]} = K_{\text{aci}} \times K = K_{\text{HIn}}. \quad . \quad . \quad . \quad . \quad (4)$$

It follows from equation (4) that

$$\frac{[A^-]}{[\text{normal}]} = \frac{K_{\text{HIn}}}{[H^+]}$$

However the ratio $\frac{[A^-]}{[\text{normal}]}$ does not in case of *p*-nitro-phenol mean the final concentration of the yellow alkaline form because the undissociated acid (aci) is also yellow.

The total concentration of the yellow form is hence $[A^-] + K \times [\text{normal}]$. If the total concentration of the indicator is [HIn], then $[\text{normal}] = [HIn] - [A^-] - [\text{aci}]$. At a given $[H^+]$ the ratio of the concentration of the colorless to that of the yellow form is:

$$\frac{[A^-] + K[\text{normal}]}{[\text{normal}]} = \frac{[A^-] - K([HIn] - [A^-] - [\text{aci}])}{[HIn] - [A^-] - [\text{aci}]} = \frac{K_{HIn}}{[H^+]}.$$

If the aci-acid is strong enough to be considered completely dissociated the usual equilibrium equation may be used:

$$\text{normal} \rightleftarrows H^+ + \text{aci.}^-$$

It is then easy to deduce the simple equation that governs the color relations.

The case is more involved when the normal form behaves perceptibly as an acid and hence enters noticeably into salt formation. We then have two acids:

$$HA \rightleftarrows H^+ + A^-, \quad \frac{[H^+] \times [A^-]}{[HA]} = K_{HA}.$$

$$HIn \rightleftarrows H^+ + In^-, \quad \frac{[H^+] \times [In^-]}{[HIn]} = K_{HIn}.$$

It may be deduced from these two relations that at equal $[H^+]$ the following relation holds:

$$\frac{[A^-]}{[HA]} \times K_{HIn} = \frac{[In^-]}{[HIn]} \times K_{HA}.$$

If [HIn] represents the concentration of the aci-form and [HA] that of the pseudo-form, then the concentration of the yellow form is $[In^-] + [HIn]$. The concentration of the colorless is $[A^-] + [HA]$. Besides we have $[HIn] = K[HA]$. Then,

$$[In^-] = \frac{K \times [HA] \times K_{HIn}}{[H^+]}.$$

The total concentration of the yellow form is hence,

$$\frac{K[HA] \times K_{HIn}}{[H^+]} + K[HA].$$

The simpler equation (4) derived on page 240 is the usual relation according to the Ostwald conception, only K_{HIn} is not the *true dissociation constant* but the *apparent dissociation constant*, i.e., the product of the true dissociation constant and the equilibrium constant for the relation of normal and aci-forms. In case of *p*-nitro-phenol this constant is very much in the direction of the normal form so that *p*-nitro-phenol is apparently a very weak acid. For ortho nitro-phenol the ratio is more favorable and the compound behaves as a stronger acid. In case of picric acid the ratio is so large that much of the aci- or ionogenic form can exist in aqueous solution in the presence of the pseudo-compound. Hence it is a moderately strong acid. With increasing apparent dissociation constant the yellow color of the aqueous solution must also increase since more of the aci-form is then present. This is actually the case. Picric acid is strongly yellow in aqueous solution, but colorless in organic solvents and hence present in the pseudo-form.

Just as has been done for *p*-nitro-phenol the relation between color and hydrogen-ion concentration could be derived for phenol phthalein and other indicators. We have here, in aqueous solution, an equilibrium between lactone form, L, and quinone form, Q.

$$L \rightleftarrows Q,$$

$$\frac{[Q]}{[L]} = K,$$

$$[Q] = K \times [L]. \quad \ldots\ldots\ldots \quad (5)$$

The quinone form dissociates into ions:

$$Q \rightleftarrows Q^- + H^+,$$

$$\frac{[H^+] \times [Q^-]}{[Q]} = K_Q. \quad \ldots\ldots\ldots \quad (6)$$

(true dissoc. constant).

It is evident from (5) that $[Q] = K \times [L]$, hence

$$\frac{[H^+] \times [Q^-]}{K \times [L]} = K_Q.$$

$$\frac{[H^+] \times [Q^-]}{[L]} = K_Q \times K = K_{HIn}. \quad . \ . \ . \quad (7)$$

Here again we find that the dissociation constant of the indicator is an *apparent* dissociation constant that is made up of the true dissociation constant and the equilibrium relation between the aci- and pseudo-compounds. In aqueous solution the equilibrium between L and Q lies in such an unfavorable position that the solution appears colorless to our eyes. Upon displacing the equilibrium with alkali the red color appears.

The change of methyl yellow, etc., is represented by the following equations:

$$\underset{\text{yellow}}{\text{Azo}} \rightleftarrows \underset{\text{red}}{\text{Quinoid.}}$$

$$\frac{[Q]}{[Azo]} = K,$$

$$[Q] = K \times [Azo], \quad . \ . \ . \ . \ . \quad (8)$$

$$Q \rightleftarrows Q^+ + OH^-,$$

$$\frac{[Q][OH^-]}{[Q]} = K_Q. \quad . \ . \ . \ . \ . \ . \ . \ . \quad (9)$$

(true dissoc. constant.)

From (8) and (9) we have

$$\frac{[Q^+] \times [OH^-]}{K \times [Azo]} = K_Q,$$

or

$$\frac{[Q^+] \times [OH^-]}{[Azo]} = K_Q \times K = K_{InOH}.$$

(Apparent dissoc. constant.)

The equations thus derived agree completely in various cases with those of Ostwald; there are the following differences:

(*a*) The dissociation constants thus derived are the products of the true dissociation constants and the equilibrium constant

giving the relation between the aci- (or baso-) and the pseudo-forms. The apparent dissociation constant thus derived may be tacitly regarded as a measure of the strength of the indicator acid or base. Probably most dissociation constants are apparent constants, according to the investigations of recent years. If we consider the dissociation constant of carbonic acid, for example, then we have:

$$\frac{[H^+][HCO_3^-]}{[H_2CO_3]} = K_{H_2CO_3}. \quad . \quad . \quad . \quad . \quad . \quad (10)$$

It is assumed that $[H_2CO_3]$ is the total carbonic acid concentration. This is incorrect because it is mainly present as the anhydride, or in other words,

$$[H_2CO_3] = K[CO_2].$$

When this value is substituted in equation (10) we have:

$$\frac{[H^+][HCO_3^-]}{[CO_2]} = K_{H_2CO_3} \times K = K' = 3 \times 10^{-7}.$$

This $K' = 3 \times 10^{-7}$ is called the dissociation constant of carbonic acid. It is really the apparent dissociation constant. The true dissociation constant is much larger because the equilibrium between CO_2 and H_2CO_3 is very much on the side of CO_2. The ratio $\frac{[CO_2]}{[H_2CO_3]}$ is about 100, so that the true dissociation constant of carbonic acid is about 100 times greater than the apparent or about 3×10^{-5}.

Similar considerations apply to ammonia. Here an apparent dissociation constant is used since it is assumed that all the ammonia is present as NH_4OH thus neglecting the equilibrium,

$$NH_4OH \rightleftarrows NH_3 + H_2O.$$

The true dissociation constant of ammonia is therefore much larger than that with which we ordinarily work.

According to the latest views of Snethlage (13) it is even an open question as to whether or not all dissociation constants

are apparent constants made up of dissociation constants and equilibrium constants for iogenic and pseudo-forms.

This idea is confirmed, for example, by an investigation made by Hantzsch on acetic acid and its derivatives; it was found that esters and salts had a different constitution, while it may be concluded with a high degree of probability that in an aqueous solution of acetic acid there is an equilibrium condition between two forms, one of which has the constitution of the ester the other of the salt. Thus we have here an equilibrium:

$$\frac{[\text{Iogenic}]}{[\text{Pseudo}]} = \text{K}.$$

Hence if it is assumed that all undissociated acetic acid is present in aqueous solution in only one form an error is made because the equilibrium between ionogenic and pseudo forms has been neglected. The true dissociation constant of acetic acid is therefore much larger than the one ordinarily used.

(*b*) A second deviation from Ostwald's theory is that according to the author's view ions do not need to have the same constitution as the undissociated acid.

Hence we arrive at a new definition of indicators, namely:

Indicators are apparently weak acids or bases whose iogenic or aci- (or baso-) form has a different color and constitution from that of the pseudo- or normal form.

In the light of this definition we may tacitly represent the reactions that occur with indicators by the following equations:

$$\text{HIn} \rightleftarrows \text{H}^+ + \text{In}^-,$$

$$\text{InOH} \rightleftarrows \text{In}^+ + \text{OH}^-,$$

where In^- and In^+ have a different constitution from HIn and InOH.

In the equations given it is assumed that the aci- or baso-compounds are so strong that they may be regarded as completely dissociated, or in other words,

$$\text{Pseudo-acid} \rightleftarrows \text{Aci}\begin{cases}\text{H}^+ \\ \text{Aci}^-\end{cases}.$$

If we now take into consideration that the dissociation constant gives the apparent value, we may write:

$$\text{Pseudo} \rightleftarrows H^+ + \text{Aci}^-,$$

$$\frac{[H^+] \times [\text{Aci}^-]}{[\text{Pseudo}]} = K_{\text{HIn}}.$$

Similar relations apply for other indicators.

The new definition is not in error because of the fact that the change of indicators is a slow time reaction; we have included in the explanation the equilibrium between the iogenic and normal forms. It may be within the bounds of possibility that the equilibrium is established slowly.

It is explained by this definition why the solid salt of phenol phthalein is red and that of *p*-nitro toluene yellow. The salts have the same color and constitution as the iogenic form, whether fully or partially dissociated. This agrees with the work of Hantzsch (8) and Hantzsch and Robertson (9), as mentioned at the beginning of this chapter, namely, that Beer's law is valid for colored salts at all concentrations. For the undissociated molecules of the salt have the same color and constitution as the ions.

The fact that phenol phthalein becomes colorless with excess of alkali does not damage this viewpoint since we have two equilibria to deal with, namely,

$$\frac{[\text{Lactone}]}{[\text{Quinone}]} = K_1,$$

$$\frac{[\text{Quinone}]}{[\text{Carboxylic acid}]} = K_2.$$

The equilibrium is slowly driven over toward the carboxylic acid side by excess of alkali.

The only difference from Ostwald's definition is that we should not say that the ions have a color different from that of the pseudo-compound, but the iogenic form has a different color. The chromic theory is included in saying that the iogenic form has a different constitution from that of the normal form.

The primary fact that governs the change of indicators is the equilibrium,

$$\text{Pseudo} \rightleftarrows \text{Ionogen.}$$

Finally we may say that the equations that were derived in the third chapter are entirely correct in the light of the new definition, and that there is no contradiction of the views of Hantzsch.

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TABLES

TABLE I

IONIZATION PRODUCT (DISSOCIATION CONSTANT) OF WATER AT DIFFERENT TEMPERATURES

	1	2	3	4
0°	0.12×10^{-14}	0.14×10^{-14}	.....	0.089×10^{-14}
18°	0.59×10^{-14}	0.72×10^{-14}	0.74×10^{-14}	0.46×10^{-14}
25°	1.04×10^{-14}	1.22×10^{-14}	1.27×10^{-14}	0.82×10^{-14}
50°	5.66×10^{-14}	8.7×10^{-14}		
100°	58.2×10^{-14}	74×10^{-14}	.....	48×10^{-14}

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TABLE II

AVERAGE DEGREE OF DISSOCIATION OF SALTS AT 18° (FOR CALCULATION OF HYDROLYSIS CONSTANTS)

Normality	Uni-univalent	Uni-bivalent
0.0001	0.99	0.98
0.0005	0.98	0.97
0.001	0.97	0.96
0.005	0.95	0.92
0.01	0.93	0.88
0.05	0.89	0.80
0.1	0.85	0.75
0.2	0.83	0.71
0.5	0.79	0.64
1.0	0.75	0.58

TABLE III

Dissociation Constants of Important Acids and Bases

Name	Temperature	Constant	Acid Exponent	Investigated by
Inorganic Acids				
Arsenic acid, First step	25°	5×10^{-3}	2.30	Luther
Arsenious acid	25°	6×10^{-10}	9.22	Wood
Boric acid	25°	6.6×10^{-10}	9.18	Lunden
Carbonic acid	18°	3.04×10^{-7}	6.52	Walker and Cormack
Second step	18°	6×10^{-11}	10.22	Auerbach and Pick
Hydrogen peroxide	25°	2.4×10^{-12}	11.62	Joyner
Hydrogen sulphide	18°	5.7×10^{-8}	7.24	Walker and Cormack
Second step	....	1.2×10^{-15}	14.92	Knox
Nitrous acid	25°	4×10^{-4}	3.40	Blanchard
Phosphoric acid	25°	1.1×10^{-2}	1.96	Abbott and Bray
Second step	25°	1.95×10^{-7}	6.7	Abbott and Bray
Third step	25°	3.6×10^{-13}	12.44	Abbott and Bray
Second step	....	5.9×10^{-7}	6.23	Corrected for activity of
Third step	....	1.0×10^{-12}	12	ions. Prideaux and Ward.
Pyrophosphoric acid	25°	1.4×10^{-1}	0.85	Abbott and Bray
Second step	25°	1.1×10^{-2}	1.96	Abbott and Bray
Third step	25°	2.9×10^{-7}	6.54	Abbott and Bray
Fourth step	25°	3.6×10^{-9}	8.44	Abbott and Bray
Sulphuric acid, Second step	25°	1.7×10^{-2}	1.77	Jellinek
		3.2×10^{-2}	1.50	Noyes and Stewart
		3.2×10^{-2}	1.50	Kolthoff
Sulphurous acid	18°	1.7×10^{-2}	1.77	Kerp and Bauer
Second step	15°	1.0×10^{-7}	7.00	Kolthoff
Organic Acids—*Aliphatic Series*				
Acetic acid	25°	1.86×10^{-5}	4.73	Lunden
n-Butyric acid	25°	1.53×10^{-5}	4.82	Jones
Iso-Butyric acid	25°	1.48×10^{-5}	4.83	Jones
Citric acid	25°	8.2×10^{-4}	3.09	Walden
		4.1×10^{-5}	4.39	Hastings and Van Slyke
Second step	18°	5×10^{-5}	4.30	Kolthoff
Third step	18°	1.8×10^{-6}	5.74	Kolthoff
		3.2×10^{-6}	5.50	Hastings and Van Slyke
Formic acid	18°	2.05×10^{-4}	3.69	Kolthoff
		2×10^{-4}	....	Auerbach and Zeglin
Fumaric acid	25°	1.01×10^{-3}	3.00	Jones
Second step	18°	5×10^{-5}	4.30	Kolthoff
Glycocoll	25°	3.4×10^{-10}	9.37	Winkelblech
Glycollic acid	25°	1.52×10^{-4}	3.82	Ostwald (1)
Hydrocyanic acid	25°	7.2×10^{-10}	9.14	Madsen
Lactic acid	25°	1.55×10^{-4}	3.81	Kolthoff
Maleic acid	25°	1.54×10^{-2}	1.81	Jones
Second step	18°	8×10^{-7}	6.10	Kolthoff
Malic acid	25°	4×10^{-4}	3.46	Walden (b)
Second step	18°	9×10^{-6}	5.05	Kolthoff
Malonic acid	25°	1.63×10^{-3}	2.79	Jones
Second step	18°	3×10^{-6}	5.52	Kolthoff

TABLE III—*Continued*

Name	Temperature	Constant	Acid Exponent	Investigated by
Oxalic acid	25°	3.8×10^{-2}	1.42	Chandler
Second step	18°	3.5×10^{-5}	4.46	Kolthoff
Proprionic acid	25°	1.4×10^{-5}	4.85	White and Jones
Pyrotartaric acid	25°	8.7×10^{-5}	4.06	White and Jones
Racemic acid	25°	1×10^{-3}	3.00	Ostwald; Walden; White and Jones
Succinic acid	25°	6.55×10^{-5}	4.18	Jones
Second step	18°	5.9×10^{-6}	5.23	Kolthoff
Tartaric acid	25°	9.7×10^{-4}	3.01	Ostwald; Walker (a)
Second step	18°	9×10^{-5}	4.05	Kolthoff
Trichlor acetic acid	18°	1.3×10^{-1}	0.88	Drucker
Valeric acid	25°	1.6×10^{-5}	4.80	Francke; Drucker
Aromatic Acids				
Benzoic acid	25°	6.86×10^{-5}	4.16	Jones
Camphoric acid	25°	2.67×10^{-5}	4.37	Jones
Second step	....	2.5×10^{-6}	5.60	Kolthoff
Cinnamic acid	25°	3.68×10^{-5}	4.43	Jones
Diethylbarbituric acid	25°	3.7×10^{-8}	7.43	Wood
Gallic acid	25°	4×10^{-5}	4.40	Ostwald (2)
Hippuric acid	25°	2.38×10^{-4}	3.62	Jones
Phenol	25°	1.3×10^{-10}	9.89	Walker (2)
o-Phthalic acid	25°	1.26×10^{-3}	2.90	Jones
Second step	....	8×10^{-6}	5.10	Kolthoff
Picric acid	25°	1.6×10^{-1}	0.80	Rothmund and Drucker
Saccharin	18°	2.5×10^{-2}	1.40	Kolthoff
Salicylic acid	25°	1.06×10^{-3}	2.97	Jones
Sulphanilic acid	25°	6.2×10^{-4}	3.21	Winkelblech
		6.55×10^{-4}	3.18	Jones

BASES

Name	Temperature	Constant	Base Exponent	Investigated by
Inorganic Bases				
Ammonia	18°	1.75×10^{-5}	4.76	Lunden
Ferrous Hydroxide	25°	6.8×10^{-10}	9.17	Whitman, Russell, and Davis.
Hydrazine	25°	3×10^{-6}	5.52	Bredig
Organic Bases—Aliphatic Bases				
Ethyl amine	25°	5.6×10^{-4}	3.25	Bredig
Diethyl amine	25°	1.26×10^{-3}	2.90	Bredig
Triethyl amine	25°	6.4×10^{-4}	3.19	Bredig
Glycocoll	25°	2.7×10^{-12}	11.57	Winkelblech
Methyl amine	25°	5.0×10^{-4}	3.30	Bredig
Dimethyl amine	25°	7.4×10^{-4}	3.19	Bredig
Trimethyl amine	25°	7.4×10^{-5}	4.13	Bredig

TABLE III—*Continued*

Name	Temperature	Constant	Base Exponent	Investigated by
Aniline	25°	4.6×10^{-10}	9.34	Lunden
Novocain	25°	7.1×10^{-6}	5.15	Kolthoff
o-Phenetidine	20°	4.6×10^{-10}	9.34	Veley (1)
p-Phenetidine	15°	2.2×10^{-9}	8.66	Veley (1)
HETEROCYCLIC BASES				
Aconitine	15°	3×10^{-8}	7.52	Veley (2)
Aconitine	15°	1.3×10^{-6}	5.88	Kolthoff
Apomorphine	15°	1.0×10^{-7}	7.0	Kolthoff
Atropin	18°	1.7×10^{-12}	11.77	Weise and Levy
Atropin	15°	4.5×10^{-5}	4.35	Kolthoff
Brucine	15°	7.2×10^{-4}	3.14	Veley (2)
Brucine	15°	9.2×10^{-7}	6.04	Kolthoff
Second step	15°	2.52×10^{-11}	10.60	Veley (2)
Second step	15°	2×10^{-12}	11.7	Kolthoff
Cevadin	15°	7.2×10^{6}	5.15	Kolthoff
Cinchonidine	15°	1.6×10^{-6}	5.80	Kolthoff
Second step	15°	8.4×10^{-11}	10.08	Kolthoff
Cinchonine	15°	1.6×10^{7}	6.43	Veley (2)
	15°	1.4×10^{-6}	5.85	Kolthoff
Second step	15°	1.1×10^{-10}	9.92	Kolthoff
Second step	15°	3.3×10^{-10}	9.48	Veley
Second step	15°	5.1×10^{-10}	9.29	Biddle
Cocaine	15°	2.5×10^{-7}	6.60	Veley (2)
Cocaine	15°	2.6×10^{-6}	5.59	Kolthoff
Codeine	15°	1×10^{-7}	7.0	Weise and Levy
Codeine	15°	9×10^{-7}	6.05	Kolthoff
Caffein	40°	4.1×10^{-12}	11.39	Wood
Colchicine	....	10^{-14}	14.0	Weise and Levy
Colchicine	15°	4.5×10^{-13}	12.35	Kolthoff
Coniine	25°	1.3×10^{-3}	2.89	Bredig
Coniine	15°	8×10^{-4}	3.1	Kolthoff
Ecgonine	15°	6×10^{-12}	11.22	Kolthoff
Emetine	15°	1.98×10^{-6}	5.70	Veley (2)
Emetine	15°	1.7×10^{-6}	5.77	Kolthoff
Second step	....	5×10^{-6}	5.30	Weise and Levy
Second step	15°	2.3×10^{-7}	6.64	Kolthoff
Hydrastine	15°	1.0×10^{-7}	7.0	Veley (2)
Hydrastine	15°	1.7×10^{-8}	7.77	Kolthoff
Isoquinoline	15°	3.6×10^{-10}	9.44	Veley (2)
Morphine	15°	6.8×10^{-7}	6.17	Kolthoff
Narceine	15°	2×10^{11}	10.7	Kolthoff
Narcotine	15°	7.9×10^{-8}	7.10	Veley (2)
Narcotine	15°	1.5×10^{-8}	7.83	Kolthoff
Nicotine	15°	7×10^{-7}	6.16	Kolthoff
Second step	15°	1.4×10^{-11}	10.86	Kolthoff
Papaverine	15°	9×10^{-8}	7.05	Veley
Papaverine	15°	8.15×10^{-9}	8.09	Kolthoff
Physostigmine	15°	7.6×10^{-7}	6.12	Kolthoff
Physostigmine	15°	5.7×10^{-13}	12.24	Kolthoff
Piperazine	25°	6.4×10^{-5}	4.19	Bredig
Second step	15°	3.7×10^{-9}	8.43	Kolthoff

TABLE III—*Continued*

Name	Temperature	Constant	Base Exponent	Investigated by
Piperidine	25°	1.6×10^{-3}	2.80	Bredig
Piperine	....	1.0×10^{-14}	14.0	Weise and Levy
Piperine	18°	5.8×10^{-13}	12.22	Kolthoff
Pilocarpine	15°	1.0×10^{-7}	7.00	Veley
Pilocarpine	15°	7×10^{-8}	7.15	Kolthoff
Second step	15°	4.2×10^{-11}	10.39	Veley
Second step	15°	2×10^{-13}	12.7	Kolthoff
Pyridine	25°	2.3×10^{-9}	8.64	Lunden
Pyridine	15°	1.25×10^{-9}	8.90	Kolthoff
Quinidine	15°	2.4×10^{-7}	6.62	Veley (2)
Quinidine	15°	3.7×10^{-6}	5.43	Kolthoff
Second step	15°	3.2×10^{-10}	9.50	Veley
Second step	15°	1.0×10^{-10}	10.0	Kolthoff
Quinine	15°	2.2×10^{-7}	6.66	Veley
Quinine	15°	1.08×10^{-6}	5.97	Kolthoff
Second step	15°	3.3×10^{-10}	9.48	Veley
Second step	....	1.3×10^{-10}	9.89	Biddle
Second step	15°	1.35×10^{-10}	9.88	Kolthoff
Quinoline	15°	1.6×10^{-9}	8.8	Veley (2)
Quinoline	15°	3.2×10^{-10}	9.5	Kolthoff
Solanine	15°	2.2×10^{-7}	6.66	Kolthoff
Sparteine	....	1.0×10^{-2}	2.00	Weise and Levy
Sparteine	15°	5.7×10^{-3}	2.24	Kolthoff
Second step	....	10^{-6}	6.0	Weise and Levy
Second step	15°	3.1×10^{-10}	9.5	Kolthoff
Strychnine	15°	1.43×10^{-7}	6.85	Veley
Strychnine	15°	1.0×10^{-6}	6.0	Kolthoff
Second step	15°	6.0×10^{-11}	10.22	Veley
Second step	15°	2×10^{-12}	11.7	Kolthoff
Thebaine	15°	9×10^{-7}	6.05	Kolthoff
Theobromine	40°	4.8×10^{-14}	13.32	Wood
Theophylline	25°	1.9×10^{-14}	13.72	Wood
Theophylline		1.2×10^{-14}	13.92	Weise and Levy

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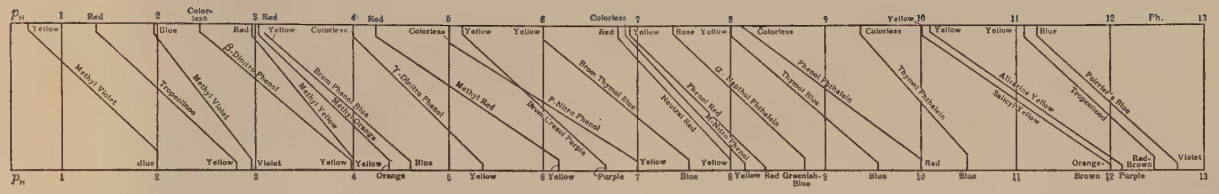
TABLE IV

Transition Range of Indicators

Indicator	Transition Range in p_H	Acid—Alkaline Color	Amount of Indicator per 10 cc.
Methyl violet	0.1– 1.5	Yellow to blue	3–8 drops 0.5%
Methyl violet	1.5– 3.2	Blue to violet	1–4 drops 0.5%
Methanil yellow	1.2– 2.3	Red to yellow	3–5 drops 1%
Thymol sulphone phthalein	1.2– 2.8	Red to yellow	2–5 drops 1%
Tropeolin 00	1.3– 3.2	Red to yellow	1–3 drops 1%
Benzo purpurin	1.3– 5.0	Blue violet to orange	1–3 drops 0.5%
β-Dinitro-phenol	2.4– 4.0	Colorless to yellow	1–4 drops 1%
α-Dinitro-phenol	2.8– 4.4	Colorless to yellow	1–4 drops 1%
Methyl yellow (dimethylaminoazobenzene)	2.9– 4.0	Red to yellow	5–10 drops 1%
Methyl orange	3.1– 4.4	Red to orange yellow	3–5 drops 1%
Tetrabrom phenol sulphone phthalein	3.0– 4.6	Yellow to blue	2–5 drops 1%
Congo red	3.0– 5.2	Blue violet to red	1–5 drops 1%
Sodium alizarine sulphonate	3.7– 5.2	Yellow to violet	1–5 drops 1%
Resazurine	3.8– 6.5	Orange to dark violet	1–5 drops 1%
γ-Dinitro-phenol	4.0– 5.4	Colorless to yellow	1–5 drops 1%
Brom cresol blue	4.0– 5.6	Yellow-blue	1–3 drops 1%
Iso-picramic acid	4.1– 5.6	Rose to yellow	1–5 drops 0.5%
Methyl red	4.2– 6.3	Red to yellow	2–4 drops 2%
Lacmoid	4.4– 6.4	Red to blue	1–5 drops 2%
Chlor phenol red	5.0– 6.6	Yellow-red	1–3 drops 1%
p-Nitro-phenol	5.0– 7.0	Colorless-yellow	3–20 drops 4%
Dibrom cresol sulphone phthalein	5.2– 6.8	Yellow to purple	1–4 drops 1%
Dibrom thymol sulphone phthalein	6.0– 7.6	Yellow to blue	1–4 drops 1%
Neutral red	6.8– 8.0	Red to yellow	2–4 drops 1%
m-Nitro-phenol	6.8– 8.4	Colorless-yellow	5–10 drops 3%
Azolitmin (litmus)	5.0– 8.0	Red to blue	10–20 drops 2%
Phenol sulphone phthalein	6.8– 8.0	Yellow to red	1–4 drops 1%
Rosolic acid	6.9– 8.0	Brown to red	1–4 drops 1%
Diortho-hydroxy-styril ketone	7.3– 8.7	Yellow to green	1–5 drops 0.5%
o-Cresol sulphone phthalein	7.2– 8.8	Yellow-purple-red	1–4 drops 1%
Brilliant yellow	7.4– 8.5	Yellow-red-brown	1–3 drops 1%
α-Naphthol phthalein	7.3– 8.7	Rose to blue	2–5 drops 1%
Tropeolin 000	7.6– 8.9	Brownish yellow to rose-red	1–5 drops 1%
Turmeric (curcuma)	7.8– 9.2	Yellow to red-brown	1–5 drops 1%
Thymol sulphone phthalein	8.0– 9.6	Yellow to blue	1–4 drops 1%
Phenol phthalein	8.2–10.0	Colorless to red	3–20 drops 1%
α-Naphthol benzene	9.0–11.0	Yellow to blue	1–5 drops 0.5%
Thymol phthalein	9.3–10.5	Colorless to blue	3–10 drops 1%
Alizarine yellow	10.1–12.1	Yellow to lilac	5–10 drops 1%
Salicyl yellow	10.0–12.0	Pale yellow-orange brown	1–4 drops 1%
Tropeolin 0	11.0–13.0	Yellow-orange brown	5–10 drops 1%
Alizarine blue S	11.0–13.0	Green to blue	1–5 drops 0.5%
Poirrier's blue	11.0–13.0	Blue to violet rose	1–5 drops 1%
Nitramine	11.0–13.5	Colorless to orange brown	1–3 drops 1%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Red
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Rose Yellow
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Colorless
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Yellow
Blue
Methyl Violet
Tropeolineo
Methyl Violet
β-Dinitro Phenol
Brom Phenol Blue
Methyl Yellow
Methyl Orange
γ-Dinitro Phenol
Methyl Red
Brom Thymol Blue
P-Nitro Phenol
Rosolic Acid
Neutral Red
Phenol Red
α-Naphtol Phthalein
Thymol Blue
Phenol Phthalein
Thymol Phthalein
Alkaline Yellow
Salicyl Yellow
Tropeoline 00
Patented Blue
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